Provincial Clinical Knowledge Topic
Parenteral Nutrition, Neonate – Inpatient
Version 1.1

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	December 2018	Version 1 of topic completed	see Acknowledgments
1.1	February 2019	Table 17 labs updated Formatting of citations updated SMOFlipid requirements (term and preterm) updated	Ssearle;Belal Alshaikh; Trudie Schimpf

Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

This topic is based on the following guidelines:

1. Corkins M, ASPEN *Pediatric Nutrition Support Core Curriculum* 2015. American Society for Parenteral and Enteral Nutrition (ASPEN) Publishers.
2. Kleinman R & Greer F. Pediatric Nutrition. Policy of the American Academy of Pediatrics. 7th edition, 2014.

For more information, see the **Parenteral Nutrition** page and pharmacy policy & procedure on AHS Internal Web (https://insite.albertahealthservices.ca/pmmc/Page17184.aspx)

- Parenteral Nutrition: Administration and Monitoring FAQ

Pharmacy:

- Parenteral Nutrition Policy
- Parenteral Nutrition Procedures

For other supporting documents, see AHS External Web:

Provincial PN Management Policy

Nursing:

- Policy: Parenteral Nutrition: Administration and Monitoring
- Procedure: Adult Parenteral Nutrition Administration and Monitoring
- Procedure: Pediatric Parenteral Nutrition Administration and Monitoring
- Procedure: Neonatal Parenteral Nutrition Administration and Monitoring

Rationale

Neonatal parenteral nutrition (PN) plays a critical role in the management of sick and growing preterm and term neonates. The primary purpose of neonatal PN is to achieve adequate (or as near adequate as possible) nutrition, thus permitting appropriate growth. Appropriate use of PN maximizes clinical benefit while minimizing the potential risk for adverse events. PN can be used as the only source of nutrition support for neonates who cannot be fed or as an adjunct to enteral feeding.

In the last few decades, there has been a significant increase in survival rates of preterm neonates, especially very low birth weight neonates. Preterm neonates are particularly at high risk of malnutrition because they are born at a time, if they had remained in utero, of rapid intrauterine brain and body growth. The impact of early malnutrition can have long-term negative effects on brain development and growth. The quality of PN is critical in providing the most adequate substrates for appropriate development.

The actual amount of nutrition must be calculated (not estimated) in neonates. The goals of nutrition support are to maintain development and growth while avoiding nutrition related complications. Nutrition requirements (enteral nutrition and parenteral nutrition) should be adjusted according to different weights and gestational age

Enteral nutrition (EN) should be gradually introduced and should replace PN as quickly as possible in order to minimize any side effects from exposure to PN. Inadequate substrate intake in early infancy can cause long term detrimental effects in terms of metabolic programming of the risk of illness in later life.

Goals of Management

Key Definitions

Parenteral Nutrition (PN): is an intravenous provision of nutritional needs for a patient who is unable to take appropriate amounts of food enterally; typical components include carbohydrates, proteins, and lipids, as well as additives such as electrolytes, vitamins and trace elements

Abbreviations and Definitions

Abbreviation	Definition
BUD	beyond use date
CHO	carbohydrate
CVAD	central venous access devices
EBM	expressed breast milk
ECMO	extracorporeal membrane oxygenation
EFA	essential fatty acid
ELBW	extremely low birthweight
EN	enteral nutrition
GIR	glucose infusion rate
ILE	intravenous lipid emulsion
IVH	intraventricular hemorrhage
LCPUFA	long-chain polyunsaturated fatty acids
LPL	lipoprotein lipase
NOHK	non-oliguric hyperkalemia
PICC	peripherally inserted central catheter
PIV	peripheral intravenous lines
PMA	postmenstrual age
PN	parenteral nutrition
PNALD	parenteral nutrition associated liver disease
PPN	peripheral parenteral nutrition
REE	resting energy expenditure
SIRS	systemic inflammatory response syndrome
SMOF	SMOFlipid®
TFI	total fluid intake
TG	triglyceride
UVC	umbilical venous catheter
VLBW	very low birth weight

Goals of Management

1. Appropriate selection of neonates who require parenteral nutrition.
2. Post-natal nutrition should be established immediately after birth for pre-term and low birth weight infants.
3. In preterm neonates, parenteral nutrition should be initiated within 24 hours of birth.
4. In term neonates, parenteral nutrition should be initiated if enteral feed is not anticipated within 2 to 3 days.
5. Enteral Nutrition (EN) should be introduced, according to site specific protocols, as soon as possible in order to minimize side effects.
6. Energy and protein target goals should be met, based on a Registered Dietitian (RD) assessment within 3 to 5 days of initiation of therapy. Appropriate ratios of protein, carbohydrate and lipid should be met.
7. Medication reconciliation shall be completed to ensure appropriate review, evaluation and reconciliation of PN when a patient is admitted or transferred on PN from another facility.
8. A Physician / Neonatal Nurse Practitioner order is required to initiate PN. Once initiated, any authorized prescriber (Physician, Nurse Practitioner, Registered Dietitian with authorization from their College, Pharmacist with additional prescribing authorization from their College) may change or discontinue a PN order.
9. Safe preparation, storage, administration and monitoring of parenteral nutrition should be facilitated by standardizing care using evidenced base practice.
10. Parenteral nutrition is considered a high alert medication and an independent double check shall be performed when preparing and administering PN as per the AHS Independent Double Check Guideline and the Pharmacy Services Independent Double Check Guideline as found on AHS Insite.
11. Appropriate infection control procedures are adhered to and aseptic technique is utilized in preparing and administering PN.
12. Medications or electrolytes shall **not** be added to the parenteral nutrition solution at the bedside.

Decision Making

Indications for Parenteral Nutrition (PN)

Parenteral nutrition is indicated when the neonate is unable to meet nutritional requirements completely by the enteral route or when the GI tract is non-functional or is not fully developed (i.e. incapable of absorbing adequate nutrients).

Descriptions of situations warranting parenteral nutrition are as follows:

1. **Prematurity**

   Premature and low birth weight neonates often have a decreased ability to digest nutrients. This may be due to decreased intestinal development, and decreased production of digestive enzymes. Preterm neonates may also have reflux, delayed gastric emptying, and gastrointestinal dysmotility making progression to full enteral nutrition (EN) feeds difficult. By 32 to 34 weeks postmenstrual age (PMA) gut motility matures and becomes more able to tolerate EN.

   Other scenarios that may require the use of PN in preterm neonate include:

   - Hypotension requiring vasopressors
   - Blood transfusions in preterm neonates are associated with decreased tissue perfusion and PN may be considered for 24 hour post transfusions if no mother's milk or donor human milk available (consent required)

2. Inability to achieve or maintain full enteral nutrition within 2 to 3 days in term neonates.

3. **Partially Functional Gastrointestinal Tract**
   - Inability to meet nutrient requirements despite maximizing enteral support
   - Neonates with gastrointestinal ostomy and/or fistula
   - Malabsorption: e.g. short bowel syndrome, villous atrophy, dysmotility syndromes
   - High risk of aspiration when small bowel feedings are not possible

4. **Non-functional Gastrointestinal Tract**
   - Meconium ileus
   - Sepsis associated paralytic ileus
   - Partial or complete bowel obstruction
   - Bowel ischemia or perforation
   - Necrotizing enterocolitis
   - In conditions that require gastrointestinal surgery— gastroschisis, omphalocele, multiple intestinal atresia's, etc. — until the enteral route is accessible.

5. **Other Indications for PN**
   - Neonates requiring major surgery
   - Neonates requiring extracorporeal membrane oxygenation (ECMO)
   - Gastrointestinal perfusion compromised by conditions such as cardiovascular or respiratory instability, congenital heart disease, use of certain medications
   - Perinatal asphyxia with organ involvement
   - Congenital Heart Disease with decreased left sided outflow
   - Respiratory failure

Contraindications for PN

PN is contraindicated when:

- Adverse reactions to any of the PN components (alternative components could be used if available) (Appendix A)

An adverse reaction to a specific component in the PN the component can potentially be omitted from the solution, or another alternative provided.

Specialized nutrition support shall be discontinued when the patient demonstrates the ability to ingest adequate oral intake or when it is determined that therapy is no longer consistent with patient goals and needs.

Potential Complications

- Adverse reactions
- Metabolic complications: (Appendix K)
  - Hypoglycemia and hyperglycemia
  - Azotemia
  - Abnormal serum and tissue amino acid pattern
  - Abnormal serum electrolytes
  - Cholestatic liver disease: Parenteral Nutrition Associated Liver Disease (PNALD) (Appendix L)
  - Hyperlipidemia and complications of lipid administration: this includes platelet dysfunction and thrombocytopenia
  - Essential fatty acid deficiency
  - Hyperammonemia
- Metabolic bone disease
- Catheter-associated complications:
  - Infection
  - Peripheral thrombophlebitis and extravasation
  - Pleural effusion or ascites
  - Air embolism
- Volume overload
- Refeeding syndrome

Process

The following steps are required in order to initiate parenteral nutrition

1. Assessment

- **Nutrition assessment**
  A nutrition assessment should be completed, which includes anthropometric, biochemical, and clinical assessment. Anthropometric assessment includes classification of gestational age and size for gestational age. It also includes determination of a Dosing Weight for the PN prescription. Dosing weight is generally based on birth weight until it is regained; otherwise it is based on actual weight. If a neonate is edematous or hydropic, a dosing weight will be determined.

- **Assessment of adverse reactions (Appendix A)**
  An assessment of adverse reactions should be undertaken prior to initiation of PN. Although rare cases of hypersensitivity reactions to various constituents of parenteral nutrition (PN) have been reported in neonates, [1, 2, 3] parenteral nutrition contains multiple nutrients and additives that could potentially trigger an adverse reaction. In the few case reports in neonates, the main components linked to adverse reactions are latex, dextrose, multivitamins, and lipid.
  - **Latex:** Latex exposure typically occurs during addition of compounds to the PN solution in Pharmacy Services. This can be minimized by alerting the PN processing area to the adverse reaction so appropriate precautions can be taken.
  - **Dextrose**: Dextrose in PN and all intravenous (IV) fluids is derived from corn therefore must be avoided in those with a corn allergy. No substitution is currently available.
  - **Lipids (ILE)**: Potential allergens associated with each ILE can be found in Appendix A. Egg, soybean, fish and olive oil may be present in the emulsion while reactions to peanut occur as a result of cross reactivity with soybean. All ILE contain egg-yolk phospholipids. Patients with severe allergic reactions to egg such as anaphylaxis reaction, may need to avoid all types of fat emulsion
  - **IV Multivitamin**: Allergic reactions linked to the multivitamin component of the PN solution have been reported in pediatrics.

2. Vascular Access

Medical staff assess and ensure appropriate and reliable vascular access. Vascular access refers to the **position of the catheter tip**. IV access sites can be peripheral or central.

a) Peripheral access – Used if parenteral nutrition is only expected to last less than 7 to 10 days or until central access is obtained. Central venous access is often pursued after 5 to 7 days if PN is expected to continue[4,5]

Peripheral Access	
Advantages	**Disadvantages**
❖ No surgical insertion ❖ Lower risk of mechanical injury (hemothorax, hydrothorax) ❖ Lower risk of air embolism ❖ Lower risk of venous obstruction	❖ Maximal osmolarity for neonates 1100 mOsm/L to minimize phlebitis and infiltration ❖ The higher the osmolarity the higher the risk of thrombophlebitis, extravasation, and occlusion

- Peripheral intravenous lines (PIV's) in the NICU typically do not last as long as central lines.
- Dextrose concentration is typically limited to 10 to 12.5% in peripheral parenteral nutrition (PPN) to prevent osmolarity from exceeding the recommended maximum. There is limited evidence to guide the recommendations on maximum osmolarity. An osmolarity of 1000-1200 mOsm/L is common.[4] PPN with osmolarity less than 1000 mOsm/L is associated with decreased phlebitis or inflammation due to infiltration[7]. To balance risk with the need to meet nutrient requirements, Alberta Health Services (AHS) has chosen a maximum of 1100 mOsm/L for neonates requiring PPN.
- For neonates with a fluid restriction, it may not be possible to meet nutrient requirements with PPN.[4]

- Lipid emulsion should be infused at the same time and into the same IV site as the amino acid/dextrose solution to reduce osmolarity when providing PPN in order to prolong the integrity of the peripheral line.[8]
- The use of heparin and IV filters reduces the phlebogenic nature of peripheral solutions.[9]
- The following formula can be used to estimate the osmolarity of the Amino Acid Dextrose Solution: (% dextrose x 50) + (% Amino Acid x 100) + (300 to 400 mOsm/L of ordered electrolytes, vitamins and minerals) (Appendix B)
- The software used to prepare amino acid dextrose solution will calculate the osmolarity based on the actual osmolarity of each ingredient added to the amino acid dextrose solution.

b) Central access – Central access should be obtained if parenteral nutrition is expected to last longer than 7 to 10 days[4]

Central Access	
Advantages	**Disadvantages**
❖ Decreased risk of phlebitis and infiltration[5]	❖ Risk of vessel thrombosis ❖ Higher risk of air embolism ❖ Greater risk of venous obstruction

- The umbilical venous catheter (UVC) is typically the first line inserted. Use of UVCs for greater than 7 days is associated with an increased risk of central line associated blood stream infections.[10]
- If central venous access is required for greater than 7 days, UVCs may be replaced with a peripherally inserted central catheter (PICC).[10]
- Umbilical arterial catheters (UAC) can be used for PN solutions, however they are typically only used for blood sampling and for monitoring blood pressure.[11]
- There is limited evidence to guide osmolarity in low-lying umbilical venous catheters (UVC) which may need to be limited in these lines. Low-lying UVC can be used for central infusions under special circumstances, particularly when IV access is critical with no other alternatives.
- Correct position of a central line should be verified radiologically at the time of placement and periodically as the neonate grows.[12]
- Examples of access devices for central infusion include UVC, PICC lines, and non-tunneled central venous access devices (CVAD) or, for longer term access, tunneled CVAD or Broviac catheters. Common insertion sites are the femoral, subclavian or jugular veins.

3. Ordering PN

a) Complete **Parenteral Nutrition (PN) Order forms** as per site specific procedures.
- Paper Based Ordering: Forward completed forms to Pharmacy as per current site procedure:
- Electronic Ordering: Follow site procedures

b) Pharmacy will distribute the prepared PN solution to the unit where it will be administered in accordance to unit specific guidelines.
Neonatal PN, as much as possible, should be protected from both ambient and phototherapy light to limit photo-oxidation during production, transport and administration. Currently no commercial product is available to completely achieve this.[13, 14]

Alberta Health Services

General Guidelines for Parenteral Nutrition

1. Starter Solutions

Starter PN solutions (Table 1) are often used for preterm neonates as the first intravenous (IV) solution ordered. Starter PN solutions provide amino acids, dextrose and calcium. Starter solutions **are meant for short term use only (the first 24 to 48 hours of life)** as sole nutrition, until PN solutions are ordered, as they do not meet all preterm neonates' nutrient requirements (Table 11). These solutions are sometimes referred to as enhanced dextrose solutions, however this is not a preferred term as it may lead to confusion with other dextrose solutions meant to provide electrolytes. It also does not give any indication that the solution contains amino acids and is therefore parenteral nutrition, which is associated with specific rules for administration which do not apply to dextrose solutions.

Early administration of starter solutions promotes positive nitrogen balance and improves dextrose tolerance in preterm infants. Amino acid administration up to recommended doses does not increase risk of metabolic acidosis. [15, 16,17,18,19, 20]

Table 1. Provincial Neonatal Starter Solutions* [15, 17, 18, 19, 20]

Components	Term Starter Amino Acid Dextrose Solution	Preterm Starter Amino Acid Dextrose Solution
amino acid % Primene™	3.3	5
dextrose (%)	10	12.5
calcium (mmol/L)	10	10

**Osmolarity may vary slightly dependent upon the products used. Osmolarity of both Starter solutions allow them to be run by peripheral or central lines.*
*Neonatal Starter Solutions will generally be provided in a **150 mL** bag for infusion. This may vary between sites.*

Table 2. Neonatal Starter Solution Nutrients Common Fluid Advancement Rates

	Term Starter (3.3% Amino Acid, 10% Dextrose and 10 mmol/L Calcium)			Preterm Starter (5% Amino Acid, 12.5% Dextrose and 10 mmol/L Calcium)		
Volume mL/kg/day	Protein (g/kg)	Dextrose (g/kg)	Calcium (mmol/kg)	Protein (g/kg)	Dextrose (g/kg)	Calcium (mmol/kg)
60	2	6	0.6	3	7.5	0.6
70	2.3	7	0.7	3.5	8.7	0.7
80	2.6	8	0.8	4**	10	0.8
90	3**	9	0.9			

**Maximum daily intake of protein in term infant*
***Maximum daily intake of protein in very low birth weight (VLBW) infant*

Points of emphasis:

- In general the term starter solution is designed for term and late preterm neonates (greater than or equal to 34+0 weeks gestation) while the preterm starter solution is for preterm neonates less than or equal to 33+6 weeks gestation.
- Parenteral 4 g/kg/day is considered the maximum daily protein requirement for VLBW neonates. 3 g/kg/day is the maximum daily requirement for term neonate.
- Consider using the term starter in preterm neonates less than or equal to 33+6 weeks when fluid intake (amino acid dextrose solution) exceeds 80 mL/kg/day.
- Maximum rate for Preterm starter solution is 80 mL/kg/day as this provides 4 g/kg/day of protein.
- No additional additives should be added to these starter solutions. Due to its short shelf half-life heparin is not included in these stocked solutions.

2. Standard Solutions

Standard PN solutions consist of predetermined amounts of dextrose and amino acids and standard concentrations of electrolytes and other PN components. Advantages to using standard PN solutions have been reported, in some but not all clinical settings.[21] These include better provision of nutrients, less prescription and administration errors, decreased risk of infection and cost savings.[22] **Standard PN solutions are appropriate for stable neonates when needs can be met with one of the available standard PN solutions**.

Table 3. Provincial Neonatal Standard Solutions [21, 22]

	Peripheral or Central Infusion			Central Infusion Only	
Components	**Low Electrolytes Standard**	**Preterm Standard**	**Term Standard**	**4% Protein**	**5 % Protein**
neonatal amino acid solution 10%	3	3	2.5	4	5
dextrose (%)	10	10	10	12.5	12.5
sodium (mmol/L)	10	30	30	30	30
potassium (mmol/L)	10	20	20	20	20
calcium (mmol/L)	7.5	15	10	15	15
magnesium (mmol/L)	1.5	2	2	2	2
phosphate (mmol/L)	7.5	15	10	15	15
acetate (mmol/L)	10	0	0	30	30
chloride	As calculated by Pharmacy				
Heparin 0.25 units/mL would be ordered separately as an additional additive to be added by pharmacy.					

3. Compounded PN prescription

Compounded PN solutions are individualized to meet a neonates requirements.

Table 4. General Guidelines for Parenteral Nutrition[4]

General Guidelines (Appendix C)		**Refer to the Sections for more Information**
1. Determine PN access as peripheral or central	Maximum Peripheral PN osmolarity is 1100 mOsm/L	
2. Determine fluid available for PN	Work collaboratively with the health care team to determine Total Fluid Intake (TFI) for PN	Fluids
3. Consider the type of nutrition and metabolic support required	Neonate may not be capable of anabolism and requires energy provision closer to resting energy expenditure (REE) for metabolic support. Energy can be increased to provide nutrition support as neonate's status improves.	Macronutrients
4. Determine the type of lipid to provide		
5. Calculate the amount of lipid needed in g/kg/day and mL/hr.		
6. Determine fluid available for amino acid/dextrose solution	Subtract feeds, lipid, and other infusions from the TFI to determine the volume available for PN. Due to fluid restrictions, insulin resistance, or altered lipid clearance, it may be necessary to begin PN at a rate less than the goal PN prescription.	

7. Determine protein requirements in g/kg/day	Special considerations are required for neonates in renal, cardiac or liver failure, or sources of increased loss (e.g. chylothorax), and during an acute phase response.	
8. Determine energy requirements in kcal/kg/day	To avoid overfeeding: • Identify total IV fluid intake and calculate energy derived from all IV dextrose solutions. • Subtract energy derived from all IV solutions from energy requirements.	
9. Determine goal initiation rates for carbohydrates (CHO) in g/kg/day and dextrose infusion rate (GIR) in mg/kg/min	Subtract energy derived from lipid and protein to determine initiation rates for CHO.	Macronutrients
10. Determine hourly rate for amino acids/dextrose and lipid solutions.	Clinical situations dictate dose and infusion rates.	Amino Acid Dextrose Solution rate may increase based on the progression of feeds
11. Determine the appropriate amount of electrolytes, trace elements and vitamins to be added to the amino acid/dextrose solution.		Electrolytes Trace Elements Vitamins
12. Determine type and amount of other additives to be added to the Amino Acid dextrose solution.		

Nutrient Requirements

1. Fluids

Neonatal fluid and electrolyte requirements are dynamic during the first 14 days of life, and therefore an understanding of the process of adaptation from intra to extra uterine life is essential.[14, 15, 23]

Table 5. Postnatal Fluid and Electrolyte Shifts [14, 15, 23]

Phase One Transition	Phase Two Intermediate Phase	Phase 3 Stable Growth
Diuresis Begins • Relative Oliguria (less than 0.5-1.0 mL/kg/hour) followed by diuretic phase • Rearrangement of fluid compartments • Caused by insensible water losses from immature skin and natriuresis continuing from fetal life	***Establishing EN Feeds*** • Decreasing insensible water losses(IWL) • Thickening of the skin • Urine volume of less than 1-2 mL/kg/hour • Low sodium excretion	***Meet Growth Needs*** • Continuous weight gain • Positive balance for water and sodium
Goals • Extracellular fluid (ECF) contracts which keeps negative water balance to less than 10% • Maintain normal serum sodium concentrations (restrict sodium intake in VLBW neonates until weight loss of ~ 6-10%) and add Na with monitoring after 48 hours of age • Sufficient urine output while avoiding oliguria (less than 0.5-1.0 mL/kg/hour) for longer than 12 hours. • Start feeds if appropriate	***Goals*** • Replace water and electrolyte losses • Advance enteral feeds as able	***Goals*** • Replace water and electrolyte losses • Fortify enteral /oral feeds to meet neonates estimated requirements to support growth.

Fluid requirements can be estimated in a variety of ways. One of the most common ways is a weight based method (Table 6). This method addresses normal maintenance and does not address fluid requirements in circumstances such as renal failure or heart failure. Several conditions require fluid intake to be adjusted.

Table 6. Usual PN Fluid Intake for Preterm and Term Neonates[14, 15]

Neonate Birth Weight	First Postnatal Week (mL/kg)					Intermediate	First Month of life growth stable(mL/kg)
	1st Day	2nd Day	3rd Day	4th Day	5th/ 6th Day		
Term Neonate	60-80	80-100	100-120	120-150	140-160	140-160	140-160
Preterm Greater than 1500 g	60-80	80-100	100-120	120-150	140-160	140-160	140-160
Preterm Less than 1500 g	60-100	80-110	100-130	130-150	140-160	140-180	140-160

**Refer to unit specific procedures as these values may differ with clinical scenario. The dietitian collaborates with the health care team regarding fluid requirements for PN.*
**Adapted from Koletzko and Groh Wargo to match current best clinical practice*

After birth, loss of interstitial fluid results in the loss of 5-10% of body weight in healthy neonates, and 5 to 15% in premature neonates. Premature neonates have large insensible water losses (IWL) (Table 7). These losses are due to the large ratio of skin to body surface area, and immaturity of the skins barrier function leading to increased evaporative fluid loss. Insensible water losses can come from a variety of sources such as fecal loss, urine, skin and respiration[14].(Appendix D) Fluid needs are higher in neonates weighing less than 1000 g, due to markedly increased IWL and decreased renal concentrating ability.

Daily IWLs are high during the first few weeks of life and decrease as the neonates' skin thickens and kidneys mature. Thickening of the neonate's skin occurs with time and also when corticosteroids are administered for lung maturation. Neonates whose mothers did not receive` antenatal corticosteroids may experience IWLs for a longer period of time, than those neonates given steroids.

Table 7. Estimated Daily Insensible Water Losses by Birth Weight (in non-humidified incubator) [4]

Neonate Birth Weight (g)	Insensible Water Loss mL/kg
Less than 750	May exceed 100
750-1000	60
1001-1250	35

Note: *Insensible water losses (IWL) are also affected by modern treatments such as humidified incubators or phototherapy[4]. Decisions regarding total fluid intake should be made by the medical team*

2. Electrolytes

Electrolyte provision is also challenging during the period of postnatal adaptation. Table 8 summarizes recommended PN electrolyte advancement based on phase of adaptation.

Table 8. PN Electrolyte Needs during Postnatal Adaptation Phases In Preterm/Term Neonates [4, 5, 23]

Neonate Birth Weight	First Postnatal Week (mmol/kg/day)			Intermediate (mmol/kg/day)			First Month of life Stable Growth (mmol/kg/day)	
	*Na	**K	Cl	Na	K	Cl	Na	K
Term Neonate	0-3	0-2	0-5	2-5	1-3	2-3	2-5	2-4
Preterm Greater than 1500 g	0-3	0-2	0-5	3-5	1-3	3-5	2-5	2-4
Preterm Less than 1500 g	0-3	0-2	0-5	2-3	1-2	2-3	2-5	2-4

** Restrict Sodium intake, during phase 1, until neonate starts diuresis.[4, 15] Once diuresis begins, adjust water and electrolytes to meet their metabolic requirements.*
*** Supplementation of Potassium usually starts after diuresis begins and requires close monitoring.*

3. Macronutrients

Optimal nutrient requirements are provided by a mixed fuel substrate in PN, including carbohydrate, protein and lipids. Ideally, carbohydrate and lipids will be used for energy substrates and protein will be used for maintaining and promoting lean body mass.

The macronutrient provision for well-balanced nutrition is in the range of:

- 15-20% protein
- 25-40% lipids
- 50-55% carbohydrate

The terms ‘non-protein energy’ or ‘non-protein calories’ are used to describe energy coming from carbohydrates and lipid only.

If energy provision is insufficient, protein will be used for energy instead; and with excess intake the energy will be deposited as fat.

a) Energy

Points of emphasis:

- Energy requirements (Table 9) in neonates fed by PN are suggested to be 5-10% lower than those enterally fed as there are no energy requirements from digestion or fecal losses due to incomplete absorption.[4]
- The resting energy expenditure (REE) represents the amount of energy expended at rest while basal metabolic rate (BMR) is more precisely defined as the REE measured just after awakening in the morning.
- Preterm neonates have energy requirements for basal metabolism and growth and also have requirements based on unique features that influence energy expenditure such as body size, age, physical activity, environmental temperatures, clinical conditions and diseases. This results in a wide range of energy requirements. (Table 10).
- Preterm energy requirements are not fully understood and require cautious application because they are based on the limited evidence available and have been developed largely upon expert opinion. This is further complicated because neonates most often receive nutrients via both parenteral and enteral routes, so energy provision is a combination of both and requirements increase as proportion of enteral feeds increases.

- Parenteral energy requirements (Table 9 and 10) are provided as recommended starting points and regular monitoring of growth and tolerance is required in order to adjust to the individual neonates needs.
- Energy requirements (Table 9 and 10) differ for compromised and critically ill neonates. During acute and chronic illness, metabolic needs are altered by a number of factors including:
  - Inflammation (increase REE)
  - Sepsis (increase REE)
  - Recovery from an infection may be associated with a prolonged increase in REE[25]
  - Sedation (decreased REE)
  - Disease condition (e.g. bronchopulmonary dysplasia can increase REE by 25%)
  - Physiological changes can also alter the utilization of the nutrition prescribed[26]
  - Unlike adults, surgery has not been shown to alter energy requirements in neonates[27]
- Growth is likely to cease during the metabolic response to illness or injury[28]. Therefore, energy requirements may be lower in critically ill neonates due to the inability to grow during this time. It seems prudent to supply at least REE and as the neonate recovers, energy can be increased to promote adequate growth.[28, 29]
- Reference values for REE in healthy preterm and term neonates during the first 5-6 weeks after birth have been reported however these values should be used with caution in ill neonates as they may not reflect energy needs for illness[30]. Furthermore, REE and BMR are difficult to measure due to the unique sleep and awake cycle and small body size in neonates. *Sleep* energy expenditure is different from REE.

Table 9. Parenteral Energy Requirements for Stable Growing Preterm Neonates[14, 83]

Energy	Preterm	Term
Total Energy Requirements*	85 to 110 kcal/kg/day*	85 to 100 kcal/kg/day
Energy Expended	40 to 60 kcal/kg/day	
• Resting Metabolic Rate	40 to 50 kcal/kg/day	
• Thermoregulation	0 to 5 kcal/kg/day	
• Activity	0 to 5 kcal/kg/day	
Synthesis	10 kcal/kg/day	
Energy Stored	20 to 30 kcal/kg/day	

**Clinical judgement is required along with continual monitoring*

Note:
1. Recommendation for parenteral energy intake in stable preterm infants varies between American Academy of Pediatrics (85-95 Kcal/kg per day) and ESPGHAN (110 – 120 Kcal/kg per day).
2. Extremely low birth weight infants require higher energy intake than other preterm infants: General guidelines:
a) Less than 1000 g: 105 to 115 kcal/kg per day
b) 1000 to 1500 g: 90 to 100 kcal/kg per day
c) more than 1500 g: 85 to 100 kcal/kg per day

Table 10. Parenteral Energy Requirements for Stable Preterm Infants [14, 83]

Energy	Preterm (kcal/kg)		
	Day 1	Day 2–7	After Day 7
ELBW* (Less than 1000 g)	40–50	75–80	105–115
VLBW* (1000 g – 1500 g)	40–50	60–70	90–100

** ELBW-extremely low birthweight; VLBW- very low birthweight*

Table 11. Parenteral Macronutrient Requirements For Preterm/Term Neonates [A, 4, 14]

Nutrient	Initial Dose		Advancement		Usual Maximum	
	Preterm	Term	Preterm	Term	Preterm	Term
Protein (g/kg/day)	3-4	2.5-3	-	-	3-4	2.5-3
Dextrose[B] Infusion (g/kg/day)	6-12	9-12	2-2.4	5	14-20	
Dextrose Infusion (mg/kg/minute)	4-8	6-8	1.4-1.7	3.5	10-14*	
Lipid[C] (g/kg/day)	0.5-1	0.5-1	0.5-1	0.5-1	3	2.5-3

**based on range required for normal growth velocity in well neonates*
[A] Clinical situations may dictate altered protein, carbohydrate, or lipid needs.
[B] These are guidelines only. Ongoing evaluation of serum glucose levels is required to evaluate glucose tolerance and guide dextrose infusion rates.
[C] Maximum lipid infusion of 0.15 g/kg/hour is suggested, which is 3.6 g/kg/day if administered continuously 24hrs per day.

b) Protein

Points of emphasis:

- Crystalline amino acids provide 4 kcal/g.
- 1 g nitrogen = 6.25 g protein
- Neonatal amino acid solutions should be used to promote normality of plasma amino acid patterns, and improve nitrogen retention and growth.[31]
- Neonatal amino acid solutions differ from solutions used in adult practice. Neonatal solutions contain increased concentrations of some essential amino acids (lysine, valine, leucine), and lower concentrations of others (phenylalanine, methionine and glycine). Some amino acids considered conditionally essential are added such as cysteine, tyrosine and taurine (Appendix E).
- Neonatal solutions have a lower pH than adult formulations which improves the solubility of calcium and phosphorus[4]. This is advantageous for preterm neonates whose calcium and phosphorous needs are high.
- Primene™ is the neonatal AHS formulary product, and is recommended for use through infancy and into early childhood[32]. Trophamine™, another pediatric specific solution, is only available by special access. It does not contain adequate amounts of cysteine, which is recommended by some experts to be added if used in neonates.
- There is no evidence to support the need to increase protein in a stepwise fashion.
- To promote efficient protein utilization and to prevent catabolism of lean body mass an energy intake of 25-40 kcal: 1 gram of protein is indicated.[4]
- Preterm neonates, particularly extremely low birth weight, commonly have an elevated BUN in the first few weeks of life due to immature renal function, and increased protein oxidation and turnover.[34, 35] There is no credible evidence that elevated BUN of the degree commonly seen in preterm neonates causes harm. Therefore, use of BUN to adjust protein intake in preterm neonates on parenteral nutrition is discouraged.

c) Carbohydrate (CHO)

Points of emphasis:

- Parenteral CHO is provided by dextrose.
- Caloric density of parenteral dextrose is 3.4 kcal/gram of dextrose.

- A significant amount of CHO may be provided through additional IV lines. All sources of CHO must be included in calculating the glucose infusion rate (GIR) and in determining the percent of carbohydrates in PN to ensure an appropriate macronutrient balance.
- A critically ill neonate may experience glucose dysregulation and require adjustment of GIRs based on stage of disease and degree of dysregulation.
- Early insulin provision to prevent hyperglycemia is NOT recommended as it may increase risk of hypoglycemia, increase intraventricular hemorrhage (IVH), parenchymal lesions and 28 day mortality.[36]
- GIR should be increased in a stepwise fashion while maintaining euglycaemia (2.6-10 mmol/L) [14, 15]
- Amino acids, leucine and arginine, stimulate insulin production which decreases blood glucose levels. Therefore optimizing protein intake will positively contribute to euglycemia.[37]
- The definition of hyperglycemia remains controversial with studies documenting levels of greater than 6.9-12 mmol/L[38]. When a dextrose/glucose infusion leads to significant hyperglycaemia (typically greater than 12-15 mmol/L), particularly in the presence of glucosuria, the attending physician may opt to start insulin therapy as a separate infusion.
- Hyperglycemia may be influenced by many factors including stress, sepsis, steroid therapy, metabolic status, excess glucose provision, and acute illness.
- A GIR of greater than 12 mg/kg/min may exceed the oxidative capacity of carbohydrate in neonates. This should be avoided especially in patients at risk of parenteral nutrition associated liver disease (PNALD).[4]
- Since dextrose is converted to fat, the provision of excess dextrose may result in fatty liver and onset of PN-associated cholestasis, hypertriglyceridemia, increased energy expenditure, increased oxygen consumption, excessive carbon dioxide production, or excessive fat deposition.
- If PN must be discontinued abruptly, depending on clinical scenario, consider using a solution with an appropriate GIR in its place such as D10W, or available standard PN solution to minimize the risk of hypoglycaemia.
- A neonate tolerating minimal enteral feeds of greater than 75 mL/kg/day of mother's milk (EBM) will receive 3.6 mg CHO/kg/min from EBM. This will likely maintain their blood glucose (BG) levels, however this does not meet energy requirements for growth and can put neonates under nutritional stress.

Use the following equation to calculate dextrose infusion rate (assumes 24hr infusion)

g/kg/day dextrose x 1000 mg/g = mg/kg/day dextrose ÷ 1440 min/day = mg/kg/min dextrose

d) Lipid

Points of emphasis:

- Intravenous lipid emulsions contribute to energy requirements and prevent essential fatty acid deficiency.
- Parenteral lipid is generally provided as a soybean oil emulsion. Intralipid® (100% soybean oil; an omega 6 fatty acid) is the parenteral lipid emulsion approved for use in Canada for neonates and children.
- 20% lipid emulsions have a lower phospholipid to triglyceride ratio than 10% products, which helps prevent depletion of essential fatty acids, lower the risk of hyperglycemia, and prevent hepatic steatosis.
- Parenteral caloric density of 20% lipid is 10 kcal/g.

- 20% lipid emulsions have an osmolarity of approximately 280-300 mOsm/L.[24]
  Note: lipids are not included in the calculation of Amino Acid Dextrose Solution PN osmolarity although when infused with Amino Acid Dextrose Solution the combined osmolarity would be less than the Amino Acid Dextrose Solution alone.
- Specialty intravenous lipids emulsions, such as SMOFlipid®, or Omegaven® may be indicated in certain clinical situations and require product specific guidelines for use. See AHS Insite page Nutrition Practice Guideline Intravenous Lipid Emulsions -Pediatric
- Lipids provide a major source of readily utilized calories.[24] Prolonged interruption of provision of long-chain polyunsaturated fatty acids (LCPUFA) may be detrimental to the neonate and lead to EFA deficiency.[24]
- Approximately 0.5-1.0 g/kg/day of Intralipid® is enough to prevent essential fatty acid (EFA) deficiency when using Intralipid® [4, 39]. In contrast, a minimum of 1.3 g/kg/day SMOFlipid® is needed to prevent EFA deficiency in preterm infant and 0.6 g/kg/day in term infants.
- Since in utero fat accretion occurs during the third trimester, preterm neonates are at increased risk for EFA deficiency presenting at birth[43]. EFA deficiency can occur after 72 hours without lipid provision in preterm neonates.[44]
- Clinical signs displayed in preterm neonates include decreased growth, flaky dry skin, inflamed skin, decreased skin pigmentation, hepatic steatosis, poor hair growth, thrombocytopenia, increased susceptibility to infections and poor wound healing. The younger the neonate the more critical the EFA signs.[38, 44, 45]
- Preterm neonates require 0.25 g/kg/day of linoleic acid and term neonates require 0.1g kg/d.
- If lipid infusion is held for a prolonged period[46] and EFA deficiency is suspected, monitor a triene: tetraene ratio. A triene: tetraene ratio of 0.05 to greater than 0.2 indicates a mild to severe deficiency respectively. [47, 48] It is important to note however that it can take an extended period of time to receive results for the triene: tetraene ratio and therefore it may not be a realistic monitoring tool if the patient is on short term PN.
- Critically ill or unstable neonates require careful initiation and advancement of lipids.
- Soybean oil emulsions may influence immune function and are associated with immunosuppressive effects.[40, 41]
- Lipoprotein lipase is inhibited by the cytokine response to stress in critical illness resulting in a decreased clearance of circulating triglycerides.[42]

Special considerations:
The use of intravenous lipids in severely impaired pulmonary function, sepsis, hyperbilirubinemia, thrombocytopenia, and small-for-gestational-age neonates requires clinical judgement.[49]

- **Sepsis**
  - It has been reported in adults that soybean oil emulsions may influence immune function and are associated with immunosuppressive effects.[40, 41] Lipoprotein lipase is inhibited by the cytokine response to stress in critical illness resulting in a decreased clearance of circulating triglycerides.[42]
  - There is limited evidence to guide the practice to decrease lipid in the face of suspected or confirmed sepsis. Careful attention to serum triglyceride (TG) levels is required in these neonates:
    - If the neonate is receiving Intralipid® and serum triglyceride (TG) levels are elevated, which may be due to the pro-inflammatory properties of Intralipid®, expert opinion suggests decreasing lipid level to 50% of the current dose or 0.5–1 g/kg/day to meet essential fatty acid (EFA) requirements and avoid excessive carbohydrate intake. Continue to monitor TG levels.

- **EFA Deficiency**
  - Since in utero fat accretion occurs during the third trimester, preterm infants are at increased risk for EFA deficiency presenting at birth[43] or more often after 72 hours without lipid provision.[44]
  - The younger the neonate the more critical the EFA signs.[45]
  - Clinical signs displayed in preterm infants include decreased growth, flaky dry skin, inflamed skin, decreased skin pigmentation, hepatic steatosis, poor hair growth, thrombocytopenia, increased susceptibility to infections and poor wound healing.[39, 44, 45]
  - Preterm infants require 0.25 grams linoleic acid/kg/day and term infants require 0.1 gram linoleic acid/kg/day. Requirements can be met with a range of 0.5 – 1 g/kg/day Intralipid®[4, 39, 83] or 0.6 (Term) – 1.3 (Preterm) g/kg/day SMOFlipid® (calculated based on requirements).
  - If lipid dose has been held for a prolonged period and EFA deficiency is suspected, monitor a triene/tetraene ratio. A triene/tetraene ratio of 0.05 to > 0.2 indicates a mild to severe deficiency respectively.[47, 48] It is important to note that it can take an extended period of time to receive results for the triene/tetraene ratio and therefore it may not be a realistic monitoring tool if the patient is on short term PN.

- **Cholestasis**
  - SMOFlipid® may be substituted for Intralipid® in neonates with cholestasis if direct bilirubin levels are greater than 50 umol/L one week apart in the absence of sepsis, and the neonate is expected to be on PN for at least another 2 weeks.
  - There is a lack of good quality efficacy and safety data in the use of SMOFlipid® greater than two weeks in this population. The possibility of coagulopathy exists therefore clinical observation and monitoring of PT/INR is required. See suggestions for monitoring on AHS Insite Nutrition Practice Guideline Intravenous Lipid Emulsions -Pediatric

- **Fat overload syndrome**
  - Fat overload syndrome is very rare in neonates. It may result from an excess accumulation of serum lipid due to high lipid infusion rate exceeding the rate of plasma clearance. Low LPL levels, low tissue carnitine and small adipose tissue mass, amongst other factors can contribute to the development of hypertrigylcedemia in preterm neonates. Onset is acute and may present with coagulopathy, hepatosplenomegaly, elevated liver enzymes, respiratory distress and thrombocytopenia. Symptoms are similar to the systemic inflammatory response syndrome (SIRS) and sepsis. Symptoms regress as lipemia clears.[5, 50]

- **Monitoring Lipid tolerance (Table 19)**
  - Triglyceride (TG) levels should be monitored while parenteral lipid is advancing to monitor tolerance.
  - Enteral feeds will contribute to TG levels, however neonates fed human milk or formula frequently have TG levels in the range of 1.7 to 2.3 mmol/L.[14, 51, 52]
  - A TG level of 2.8 mmol/L during lipid infusion is considered the upper limit in newborn, premature and term neonates.[4, 14, 39]
  - Once enteral feeds are advancing and PN lipids are at target or decreasing, TG levels may no longer be required for monitoring unless clinical scenario dictates e.g. development of clinical deterioration could compromise lipid tolerance.
  - Triglycerides may be elevated (greater than 2.8 mmol/L) due to a number of factors[4, 14, 39]:
    - Lipid or carbohydrate infusion rate exceeding the rate of plasma clearance,
    - Inflammation and/or sepsis,
    - Metabolic dysregulation,
    - Limited lipoprotein lipase (LPL) activity due to prematurity,
    - Levocarnitine Deficiency
  - If TGs continue to be elevated above 2.8 mmol/L provide at least 0.5–1 g/kg/day Intralipid® or 1.3 g/kg/day (Preterm) and 0.6 g/kg/day (Term) SMOFlipid® to prevent EFA deficiency.[14, 39]
  - As TGs are normalized, advance lipids cautiously by 0.5–1 g//kg/day to reach goal rate.[39]
  - Levocarnitine: Supplement with levocarnitine 5 to 10 mg/kg/day in the PN to enhance fatty acid oxidation.[4, 39, 53]

4. Micronutrients

a) Other Electrolytes

The general guidelines for sodium, potassium and chloride are mentioned with the fluid section. Electrolytes can be adjusted according to each neonate's individual needs.

Table 12. Usual Electrolyte Requirements in Preterm/Term Neonates [4, 5]

	Daily Intake	
Electrolyte	**Preterm (mmol/kg/day)**	**Term (mmol/kg/day)**
sodium	2 to 5	2 to 5
potassium	2 to 4	2 to 4
calcium	1 to 2	0.25 to 2
phosphorous	1 to 2	0.5 to 2
magnesium	0.15 to 0.25	0.15 to 0.25
acetate	As needed to maintain acid-base balance	

General Guidelines for electrolyte additions to PN prescriptions

Electrolytes should be ordered as ions in AHS facilities (e.g. Na vs NaCl which is the salt). Ordering electrolytes as ions allow for adjustments to be made when individual salts are in short supply. The salts that will be used by pharmacies within AHS are as follows:

Table 13. Electrolyte Salts available for PN Solutions[4, 5]

sodium chloride	potassium chloride	calcium gluconate
sodium acetate	potassium acetate	magnesium sulfate
sodium phosphate	potassium phosphate	

a) **Sodium**

- Addition of sodium to PN is restricted during the first 48 hours of life until diuresis begins.[4, 15]
- Preterm neonates have immature kidneys at birth and most very low birth weight (VLBW) neonates are renal salt losers between 2-6 weeks of age. Excretion of sodium is increased once diuresis begins. A normal sodium level after the first week of life is beneficial for growth and neurodevelopment.[14, 15]
- Increase sodium to goal, (Table 12) based on serum and/or blood gas values, fluid status, and renal function.
- Extremely premature neonates may have higher sodium requirements of 5 to 7 mmol/kg/day. A maximum safe concentration for sodium supplementation in PN is 154 mmol/L, the equivalent of normal saline.

b) **Potassium**[14, 15]

- Addition of potassium to PN will need to be delayed until urine output is well established (greater than 1 mL/kg/hr) and serum potassium is within normal limits
- Increase potassium to goal (Table 12) based on serum and/or blood gas values, fluid status, and renal function.
- Non-oliguric hyperkalemia (NOHK) is a common early complication of extremely preterm neonates. Neonates with NOHK have a serum potassium level greater than or equal to 6.5 mmol/L during the first 72 hours of life in the presence of urinary output greater than 1 mL/kg/hr. NOHK is partly due to a shift of potassium from the intracellular space into the extracellular space associated with an immature function of Na/K ATPase activity.[54]
- Potassium is generally limited to 60 mmol/L in peripheral lines, and 80 mmol/L in central lines for PN, however refer to the AHS Insite AHS Provincial Parenteral Drug Manual potassium monographs for up to date limits. The maximum potassium administration rate as continuous infusion is typically 0.25 mmol/kg/hour however rates up to 0.5 mmol/kg/hour can be used but require continuous ECG or cardiac monitoring. Ensure all sources of potassium are included in rate calculations.

c) **Calcium and Phosphorus**

- Since maximum accretion rates of calcium and phosphorus occur during the last trimester, it is important to provide adequate amounts of calcium and phosphorous to neonates and especially preterm neonates to decrease the risk of metabolic bone disease.[4, 23, 55]
- It is difficult to provide recommended amounts of calcium and phosphorus, especially when the amount of sodium and potassium in PN is minimized. Calcium and phosphorus solubility in neonatal PN solutions depend on their amounts, the total volume of the PN bag, the calcium: phosphorus ratio, pH, temperature, the amino acid concentration, and the type of commercial amino acid product used. The ideal calcium-

phosphorus molar dosing ratio to promote optimal mineral retention and tolerance is 1-1.4 mmol Ca: 1mmol Phosphorus.[14, 15]

- Calcium and phosphorus solubility is enhanced by the higher acidity of neonatal amino acid solutions, addition of cysteine, and higher amino acid concentrations[4]
- The amount of phosphorus that can be added to PN depends on the amount of sodium and potassium. Calcium is provided as calcium gluconate, and therefore does not depend on the availability of other electrolytes.
- Calculations and graphs are used to determine approximate calcium and phosphorus compatibility of neonatal amino acid solutions. Consult a PN pharmacist if guidance is required.(Appendix F)
- Provide recommended amounts of Calcium and Phosphorus (Table 12), as solubility allows
- Neonates born small for gestational age or with intrauterine growth restriction are at risk of refeeding syndrome due to rapid growth and increases in lean tissue.[5, 14, 56] Phosphorus needs may be increased as a result.

d) **Magnesium**

- Magnesium plays a crucial role in bone strength, muscle and nerve function, and calcium and phosphorus homeostasis.
- If magnesium sulfate was administered to mother during labour, magnesium should not be added to PN until serum magnesium is obtained. Magnesium sulfate, given for treatment of preterm labour or preeclampsia, can cross the placenta and cause hypermagnesemia. Serum magnesium levels should normalize in 2-5 days depending on the neonates' renal function and level of hypermagnesemia.[4]

e) **Acetate**

- **Acid-Base Homeostasis and Disturbances**[57]
  - For normal cell function, acid-base balance via metabolic and respiratory pathways must be maintained. This balance is regulated via the lungs, kidneys and chemical buffers. (Appendix H)
  - If the kidneys or lungs are immature or have decreased function, the neonate may not be able to compensate for the acid base disturbance and treatment of the underlying cause should be addressed.
  - Acids are defined as substances that can donate a hydrogen ion (H^+) and a base is a substance that can accept a hydrogen ion. pH is the concentration of H^+ in solution. Most H^+ in the body occurs as products of cellular metabolism.
    - Acidemia is a process associated with an increase in H^+ ion concentration resulting in decreased pH.
    - Alkalemia is a process associated with decreasing H^+ ion concentration resulting in increased pH.
  - The carbonic acid/HCO_3^- buffer system is the body's primary extracellular buffering system
    - $H_2O + CO_2 \leftrightarrow H2CO_3^- \leftrightarrow H+ HCO_3^-$
  - Hemoglobin buffers proteins
  - Lungs regulate pCO_2, allow for CO_2 excretion and can compensate for acid-disturbance
  - If the kidneys or lungs are immature or have decreased function, the infant may not be able to compensate for the acid base disturbance and treatment of the underlying cause should be addressed.

- **Management of Non Anion Gap Metabolic Acidosis in parenteral nutrition**
  - For non-anion gap metabolic acidosis, use of acetate in PN is recommended.
  - Acetate is converted to bicarbonate in the liver and should not be used in liver failure as it can worsen acidosis. In this case, the acidosis may be treated by the medical team using bicarbonate as a separate infusion or medication.
  - Bicarbonate itself cannot be added to PN solution as it will precipitate the calcium and phosphorus
  - The amount and the type of amino acid solution used to prepare the PN will also influence the amount of acetate required. The higher cysteine content of Primene™ or individual supplementation of cysteine may increase the need for acetate in newborn neonates receiving parenteral nutrition [58]

- **Management of Saline Responsive Metabolic Alkalosis in Parenteral Nutrition**
  - Sodium and potassium can be added as chloride to replace loses or limit acetate (bicarbonate) source

b) Trace Elements

For neonates requiring PN longer than 1 month it is important to monitor serum levels of trace elements monthly, as able, and observe for clinical signs of deficiency or excess. Provide trace element requirements (Table 14) using the AHS trace element solution for preterm and term neonates. (Appendix I)

Table 14. Recommended Parenteral Trace Element Dose for Preterm / Term Neonates[23, 53, 59]

Trace Element	Preterm PN Less than 3 kg Requirements* (mcg/kg/day)	Term PN 3 -10 kg Requirements* (mcg/kg/day)	AHS Trace Element Solution (mcg/0.5 mL)**
zinc**	400	50-250	250*
selenium	1.5-4.5	2	2
copper	20	20	20
iodine	1	1	1
manganese	1	1	Contaminant therefore none added
molybdenum	0.25	0.25	
chromium	0.05-0.3	0.2	
iron	200-250***	100***	Not added to PN

Preterm and Term Dose 0.5 mL/kg, Maximum 10 mL/day.
***Add additional 150+ mcg/kg zinc to PN for Preterm Neonates to meet their daily zinc needs*
****Administer iron external to PN. Use only if PN greater than 2 months, no iron if PRBC in 14 days[60]*

Commercially manufactured trace element preparations do not currently provide trace elements in required doses[53]. AHS has developed a custom trace element solution to meet the needs of Preterm and Term Neonates. Adjust the dose of the AHS custom trace element solution and/or dose trace elements individually to meet the neonate's needs.

Table 15. Individual Trace Elements available for PN Solutions [4, 5]	
Element	**Availability**
zinc	✔
selenium	✔
copper	✔
chromium*	✔
iodine	✔
manganese	X
molybdenum	X
**Check with pharmacy if available on site*	

A. Zinc

- Zinc is a cofactor in metabolism of protein, lipids and carbohydrates, growth and cell differentiation. The need for zinc increases with severe diarrhea, inflammatory/ malabsorptive disorders, abnormal fluid losses (stomas, fistulas, gastric drainage) and high urinary output.
- Preterm neonates require an additional 150 mcg/kg/day of zinc added to the PN solution individually in order to meet their daily zinc requirements of 400 mcg/kg/day.

B. Selenium

- Selenium acts as an antioxidant and protects against membrane oxidative damage. It is a cofactor in antioxidant enzymes, involved in thyroid hormone metabolism and is a cofactor for protein and DNA synthesis.
- Preterm PN requirements for selenium range from 1.5 - 4.5 mcg/kg/day. (Table 15). The AHS Neonatal/Pediatric Trace element solution provides 2 mcg/kg/day in 0.5 mL solution
- Metabolic stresses such as inflammation, surgery, sepsis, or situations with high losses (chylothorax) decrease body stores of selenium.[61] Selenium deficiency can be corrected with increases of parenteral or enteral selenium above the standard trace solution to 5 - 7.5 mcg/kg/day.[62] Recheck selenium level after 1 month, or sooner if clinically relevant, and adjust dose as needed.

C. Copper

- Approximately 80% of copper given parenterally is excreted in the bile[63]
- Previous recommendations suggested removal of copper from trace solution in the presence of cholestatic liver (Appendix I) disease, however more recent literature has found that in order to prevent deficiency addition of 20 mcg/kg/day of parenteral copper can be given safely to neonates with cholestatic liver disease.[61, 63, 64, 65] (Appendix L)
- It could be harmful to reduce the amount of copper given to cholestatic preterm neonates as it increases their risk for deficiency.[61]
- Preterm neonates with cholestasis requiring PN greater than 1 month should have serum copper checked monthly. If levels are normal, continue supplementation, if levels are high decrease copper to 10 mcg/kg/day or hold the dose and continue to monitor levels.[59]
- Preterm and term neonates with excessive GI losses may need an additional 10 to 20 mcg/kg/day of copper to compensate for losses.[59, 61, 66]

D. Iodine

- Iodine has a role in thyroid function involving metabolism of protein and energy.[53,67,69,70]
- The AHS trace element solution contains 1mcg of iodine in 0.5 mL of solution. This is the amount recommended for preterm neonates on long-term PN in order to prevent deficiency.[14, 53, 59]

- Extremely low birth weight neonates and neonates with short bowel syndrome on long-term TPN may require additional iodine.[71, 72]
- Check urine iodine or thyroid function for neonates on PN greater than 1 month.[73]

E. Manganese / Molybdenum / Chromium

- Since 90% of Manganese is excreted through bile, and high levels of manganese can lead to neurological and hepatic complications, caution should be used when supplementing manganese parenterally. The retention of parenteral manganese in the preterm neonate is considered to be 100%, the risk of deficiency is low, and with increasing evidence for toxicity trace element solutions should not contain manganese.[74, 75]
- Molybdenum exists as a contaminant in PN solutions and is therefore not necessary to be supplemented in short-term PN (less than 1 month).
- Chromium exists as a contaminant in PN solutions and is therefore not necessary to be supplemented in short-term PN. Monitor serum levels in long-term PN (greater than1 month) and supplement only if deficient. Since chromium is excreted in the urine, use caution when supplementing patients with renal impairment.[60, 75] Elevated serum levels of chromium have been associated with reduced glomerular filtration rate (GFR) suggesting nephrotoxicity.[61,76]

F. Iron[4]

- Iron is involved in many body processes such as DNA replication, cellular energetics, oxygen delivery, neurodevelopment, and T-cell immunity
- Iron status can be influenced by blood loss, iron intake and erythropoiesis. Inflammation, iron overload and red blood cell infusions can contribute to increases in serum ferritin concentration. One blood transfusion can provide 3 months of iron requirements.[4, 77]
- Since iron is not included in trace element preparations, patients on PN will need an alternate source of iron. The enteral route is the preferred route for administering iron if it can be tolerated and absorbed. Parenteral iron can be administered separately from PN for those unable to receive enteral supplementation. IV iron may be required if a patient remains NPO for more than 2 months.[59, 60]

c) Vitamins

- Multivitamins, especially thiamine, should be administered daily and never omitted from the PN prescription.
- Urinary excretion of water soluble vitamins administered parenterally is increased. The parenteral doses are 2– 5 times greater than the oral nutrient requirements.[53]
- Losses of riboflavin and ascorbate occur with clear IV tubing and phototherapy; therefore it is recommended that dark line PN bag covers be used.[78]
- Use of adult parenteral multivitamins in neonates less than 1500 g is not recommended. These vitamins contain the additives propylene glycol, polysorbate 80 and/or polysorbate 20, which may be toxic to young neonates.[64]
- There are currently no commercially produced preterm parenteral multivitamins available. Provide PN vitamin requirements for preterm and term neonates using Multi-12K1 Pediatric.[64] (Table 16)

Table 16. Recommended dosing of Multivitamins (Multi-12®K_1Pediatric Solution)

Vitamin	Preterm PN Requirements (units/kg/day)	Preterm Dose (2 mL/kg/day)	Term PN Requirements (units/day)	Term (5 mL/day) Recommended & Maximum dose
thiamine (B_1) mcg	200 to 350	480	1200	1200
riboflavin (B_2) mcg	150 to 200	560	1400	1400
niacin (B_3) mg	4 to 6.8	6.8	17	17
pyridoxine (B_6) mcg	150 to 200	400	1000	1000
folate mcg	56	56	140	140
vitamin B_{12} mcg	0.3	0.4	1	1
pantothenic acid mg	1 to 2	2	5	5
biotin mcg	5 to 8	8	20	20
vitamin C mg	15 to 25	32	80	80
*vitamin A units	700 to 1500	920	2300	2300
vitamin D units	40 to 160	160	400	400
**vitamin E units	2.8 to 3.5	2.8	7	7
***vitamin K mcg	10***	80	200***	200

** vitamin A: 1 mcg RE = 1 mcg all-trans retinol = 3.33 IU vitamin A.*
*** vitamin E: 1 equivalent = 1 mg α tocopherol.*
**** vitamin K: + 500 to 1000 mcg IM/IV at birth based on birth weight* (Parenteral monograph is weight based so this value will vary)
[1] *Usual Parenteral Vitamin Requirements in Preterm and Term Neonates*[53]

- Preterm neonates vitamin requirements are met with 2 mL/kg and term neonates' requirements are met with 5 mL/day of the Multi 12 K_1 pediatric solution. When ordering PN, for neonates the recommend dose is 2 mL/kg. Pharmacy will ensure a maximum dose of 5 mL/day is provided for any neonate over 2.5 kg.
- **Some medications may alter vitamin/mineral requirements. Examples of medications that may alter micronutrient levels are as follows:**
  - Amphotericin (urinary loss of potassium and magnesium).
  - Hydrochlorothiazide (urinary loss of sodium, potassium, chloride, magnesium, phosphorus, zinc, riboflavin and bicarbonate and causes calcium retention).
  - Corticosteroids (urinary loss of potassium, zinc, and vitamin C).
  - Furosemide (urinary loss of potassium, phosphorus, sodium, chloride, magnesium and calcium).
  - Spironolactone (urinary loss of sodium, chloride, and magnesium and retention of potassium).

d) Additives

A. Levocarnitine

- Levocarnitine facilitates the oxidation of long-chain fatty acids (acyl compounds) in the mitochondrial matrix by transporting them across the mitochondrial membrane[4]
- Levocarnitine is stored in fetal tissue in increasing amounts over the latter part of gestation; therefore, tissue stores at birth are related to gestational age[4]
- Levocarnitine is considered conditionally essential in preterm neonates and neonates receiving exclusive PN.[4]
- Neonates receiving PN without supplemental levo-carnitine may have decreased carnitine levels.[4]
- Levocarnitine supplementation is required to optimize fatty acid oxidation, lipid tolerance, nitrogen balance, and weight gain.[4]
- Levocarnitine should be supplemented at 5-10 mg/kg/day, as needed, in preterm or term neonates less than 5 kg if no enteral source is provided.[4, 39, 53]

B. Arginine [79, 80, 81]

- Arginine is an essential amino acid for the fetus and neonate. It can be synthesized from other amino acids however, this is dependent on dietary protein supplied.
- It is a precursor for synthesis of nitric oxide, creatinine, polyamines, urea, ornithine, proline and glutamate.
- Nitric oxide is important for normal GI function as a regulator of vasomotor function, a neurotransmitter to regulate peristalsis, an inhibitor of leukocyte adherence and modulator of inflammatory responses in the intestine.
- Arginine stimulates secretion of insulin and growth hormone and may be necessary for tissue growth and normal physiologic function.
- Although plasma arginine concentrations have been found to be decreased in preterm neonates with necrotizing enterocolitis (NEC), further research is needed before arginine supplementation can be recommended for neonates at risk of NEC.[14, 23, 79, 82]

C. Heparin

- Heparin stimulates the release of lipoprotein lipase but has not been found to improve lipid utilization.[14, 64]
- Heparin may reduce the adherence of fibrin sheath around the catheter, and may reduce phlebitis, and increase catheter patency in peripheral IVs.[9]
- A heparin dose of 0.5 units/mL added to neonatal PN may be as effective as 1 unit/mL at enhancing catheter patency.[4]
- Based on consensus, heparin administration within AHS is recommended at a concentration of 0.25 units/mL in central and peripheral lines as the lowest effective dose for reducing phlebitis and improving catheter patency. This should be added as an additive to the PN solution.
- Because starter solutions are only intended to be used for the first 24 hours, they are premade by pharmacy and stored on the units with beyond use date (BUD) of 9 days. Heparin is only stable for 24 hours in PN therefore it is not added to starter solutions by pharmacy. Heparin can be "Y-in" when starter solutions are used via central venous access.
- Risk from "Y-in" heparin when starter solutions are used for less than 24 hours and via peripheral venous access may outweigh the benefit from heparin.

D. Ranitidine

- Ranitidine increases gastric pH.[82]
- May increase the proliferation of pathogens thought to be involved in the development of NEC and infections. For this reason ranitidine, should be avoided particularly in preterm neonates.
- Ideally, if required this should be administered and considered as a separate medication and not included in PN.

E. Medications and Blood Products

- Certain medications are not compatible with parenteral nutrition as they will disrupt the stability of the solution. Such medications cannot be run through the same line or lumen. If necessary, medical staff may have to flush medications into lines manually rather than run them through an IV pump.
- In general, medications should not be added to PN bags unless absolutely necessary and should only be added in pharmacy (never at bedside).[1] This will help avoid compatibility issues, medication dosing errors with PN rate changes and delayed discontinuation of medications.
- Information on specific drug compatibilities is available through Lexicomp. Discuss any medication compatibility concerns with local pharmacists or use the following link for

drug compatibilities. Medication compatibility questions can also be directed to the Unit Clinical Pharmacist (or Inpatient Dispensary Pharmacist during off hours): https://insite.albertahealthservices.ca/Main/assets/tms/phmc/tms-phmc-pediatric-tpn-drug-compatibility-chart.pdf
Medication compatibility questions can also be directed to the Unit Clinical Pharmacist (or Inpatient Dispensary Pharmacist during off hours)

- Refer to – Carbohydrate considerations (*see section 3. c) Carbohydrate*) when PN is interrupted during administration of drugs incompatible with PN solutions.
- Blood products are not compatible with PN as the elevated dextrose solution can burst red blood cells in a slow-moving IV. PN is stopped during transfusions unless it is run through a separate line.

Monitoring and Evaluation

- Regular monitoring of PN efficacy by assessing both clinical data (infectious symptoms, appearance of line insertion sites) and laboratory testing is necessary for all patients on PN. Monitoring allows for evaluation of individual patient's needs and helps identify and mitigate complications that may develop[4] (Appendix K). Laboratory tests are essential but should be done judiciously in the NICU or Intensive Care Nursery (ICN) due to the low blood volume of neonates. Laboratory tests should be limited to seeking essential information that would influence the prescription of PN and/or the addition of oral supplements.
- A recommended monitoring schedule is outlined in Table 17. Based on the disease trajectory and clinical status of the patient, bloodwork may be ordered more or less frequently. Stable patients on long-term PN will require less frequent monitoring[4].
- Monitor weight, fluid balance (intake and output), laboratory values, and physical appearance of the neonate (dry mucous membranes, edema) to assess and adjust fluid provided by PN and EN[4]. IV medication volume may influence PN fluid allowance. Additional IV fluids may be required to replace ongoing fluid losses.
- Blood draw protocols, guidelines and pediatric reference intervals vary between zones. Please refer to zone specific information at the following link: Laboratory Test Directory and Collection Information

The following tables show the monitoring and ongoing assessment that should be implemented during the period of administration of PN:

Table 17. Suggested Laboratory Monitoring Schedule for Neonates on PN [4, 14]

Test		First week (Initial Stabilization)	Stable PN	Comment
Glucose		Every 6 to 24 hours	Weekly	As per protocol
Sodium, Potassium, Chloride, Bicarbonate, Ionized Calcium (via capillary blood gas)		Daily while increasing fluid intake (suggested first 3 days)	Weekly	Obtain from blood gas if no other blood work required
Phosphorous, Magnesium		Initially at the end of the first week of life	Weekly	
Triglycerides	Preterm Less than 32 weeks	With each increase in lipid dose	Weekly	Twice weekly if ill
	Preterm greater than 32 weeks	After achieving 2 g/kg/day lipid dose		
Bilirubin, Direct Bilirubin, Total		As indicated	Weekly	Evaluation for Cholestasis if DB greater than 34 mmol/L DB greater than or equal to 50 mmol/L and on SMOFlipid please follow lab SMOFlipid guidelines
Creatinine, Urea				When clinically indicated
Liver Panel - (Alanine aminotransferase Alkaline Phosphatase, Aspartate Transaminase Gamma Glytamyl Transferase)		After 2 weeks on PN	Every 2 to 4 weeks while on PN	
Trace elements*			After one month on non-progressing enteral nutrition	When clinically indicated
Urine Glucose		Daily when serum glucose is elevated	When serum glucose is elevated	
C-Reactive Protein, Pre- Albumin				When clinically indicated

Additional Monitoring (as clinically indicated)

- CBC with differential: when clinically indicated every 2 to 4 weeks while on PN.
- PT (INR): when on SMOFlipid or Omegevan for more than 2 weeks and when clinically indicated.
- *Serum copper, serum zinc, serum selenium, serum chromium, urine iodine (or TSH): every 1 month with non-progressing enteral nutrition.
- Carnitine Profile (including Ester/free ration): every 3 to 6 months if supplemented parenterally, otherwise check annually.

Table 18. Additional Physical Monitoring and Assessment			
	First Week	**Stable PN**	**Comment**
Weight	Daily	Daily	
Length	Weekly	Weekly	
Head Circumference	Weekly	Weekly	
Note: *This is a guideline only, monitoring requirements may differ depending on the infant and the clinical situation.*			

- Monitoring may be required more frequently if clinically indicated. More stable infants may require less frequent monitoring.
- Blood gas samples may be acceptable for monitoring electrolytes to minimise blood sampling, but should not replace serum monitoring until infant is stable on PN.
- IV Lipid Infusion is based on serum Triglyceride Levels

Table 19. Additional Monitoring and Assessment Triglyceride Levels [4,19]		
Triglyceride Level	**Action**	**Triglyceride Level**
Less than 2.8 mmol/L	• Advance lipid intake as normal. • Assess TG 24 hours after. When lipid intake is satisfactory, assess triglyceride once weekly.	Less than 2.8 mmol/L
2.8 to 4.5 mmol/L	• Decrease lipid intake by 50% or to the previously tolerated level until next check.	2.8 to 4.5 mmol/L
Greater than 4.5 mmol/L	• Stop lipid infusion for 24 hours. • Check TG level in 24 hours.	Greater than 4.5 mmol/L

Note:

- Start lipid at 0.5 to 1 g/kg/day in Infants less than 750 g at birth or small for gestational age (less than 3rd percentile) and advance by 0.5 g/kg/day to 1 g/kg/day.
- Start lipid at 1 to 2 g/kg/day in neonates with a birth weight greater than or equal to 750 g at birth and advance by 1 g/kg/day.
- Maximum lipid intake in preterm infants is 3 g/kg/day.
- To prevent essential fatty acid deficiency in:
  - Preterm infants: aim to provide minimum lipid intake of 1 g/kg/day of Intralipid or 1.3 g/kg/day SMOFlipid (0.25 linoleic acid).
  - Term infants: aim to provide minimum lipid intake of 0.5 g/kg/day of Intralipid or 0.6 g/kg/day SMOFlipid (0.1 linoleic acid).

Weaning and Discontinuing Parenteral Nutrition

a) Minimal Enteral Nutrition

- It is advantageous to begin early provision of enteral nutrition as soon as the infant is hemodynamically stable, typically within 24 hours of life.[2] Lack of enteral nutrition may diminish gastrointestinal function and structural integrity by decreasing hormonal activity, growth of intestinal mucosa, lactase activity, nutrient absorption and motor maturation. Delaying the introduction of enteral nutrition may compromise later feeding tolerance, growth and hospital stay.[84]
- "Minimal Enteral Nutrition" also known as "enteral prime" or "trophic feeds" is a method of feeding that is used to induce, enhance and maintain gut maturation before starting regular feeding. [84] Its primary purpose is not for nutrient delivery, as nutrition is maintained by parenteral support.

    - **Initiation of Trophic Feeds**
        - Initiate trophic feeds of mother's milk as per site specific recommendations as tolerated and maintain for at least 24 hours.
        - If mother's milk is not available use donor human milk (DHM) if the infant meets requirements for use. If requirements for DHM are not met and mother's milk is not available, use appropriate infant formula depending on the clinical scenario for trophic or enteral feeds.
        - Duration of trophic feeds is not specifically defined in the literature, but priming can be continued for several days or longer.
        - Trophic feed volume may not be included in the total fluid intake (TFI).

b) Transition from Parenteral to Enteral Feeds

- Some factors that need to be considered when determining readiness for transition from parenteral to enteral feeds include: stable clinical condition, neurological status and gastrointestinal function.
- This time of transition varies depending on gestational age and clinical condition, which usually takes days but may last for months, during which time the infant may be fed a combination of PN, EN (tube feeds) and possibly even some oral feeds. This process involves a step-wise progression of PN to EN with assessment of tolerance and adequacy of nutrient needs at each step.

    As the protein provided in the formula or breastmilk is usually less than the PN prescription, combining the two modes of feeding will provide less total protein overall. In this case, the PN prescription will need to be adapted to ensure the total protein received by the neonate meets their need.

    Adjustment of all macronutrients, including lipid and carbohydrates, to maintain balanced calorie intake is important during this transition.
    The macronutrient provision for well-balanced nutrition is in the range of:
    - 15-20% protein
    - 25-40% lipids
    - 50-55% carbohydrate

- If "minimal enteral nutrition" is tolerated, and infant is ready to transition from PN to EN, increase feeds according to site specific recommendations.

- When transition from PN to EN is prolonged >1 month, reassess the adequacy of vitamins, minerals and trace elements provided by all sources and adjust prescription as needed to ensure needs are met.
- PN should be continued until infant is tolerating adequate amounts of enteral nutrition[1] about 125 to 150 mL/kg/day, and advancement to full feeds is expected within 24 to 48 hours. PN may be discontinued once enteral feeds reach 100 mL/kg/day (or as per site specific guidelines) to decrease the risk of line associated infection. The transition from PN to enteral nutrition requires close monitoring to minimize nutrition deficits during this time.

Order Set: Neonatal Parenteral Nutrition (PN) Order Set

Order Set Keywords: neonate. TPN

PN Orders
Refer to AHS Internal Web for Neonatal 2-in-1 Starter Parenteral Nutrition (PN) Order
Refer to AHS Internal Web for Neonatal 2-in-1 Standard Parenteral Nutrition (PN) Order
Refer to AHS Internal Web for Neonatal 2-in-1 Compounded Parenteral Nutrition (PN) Order

Laboratory Investigations

Draw the following labs on Date: _____ *(yyyy-Mon-dd)* Time _____ *(hh:mm)*

Hematology
- ☐ Complete Blood Count (CBC) with differential

Chemistry
- ☐ Sodium
- ☐ Potassium
- ☐ Chloride
- ☐ Bicarbonate
- ☐ Calcium – Ionized
- ☐ Phosphate
- ☐ Magnesium
- ☐ Triglycerides
- ☐ Glucose Random
- ☐ Bilirubin – Direct
- ☐ Bilirubin – Total
- ☐ Creatinine
- ☐ Alanine Aminotransferase
- ☐ Aspartate Transaminase
- ☐ Alkaline Phosphatase
- ☐ Gamma Glutamyl Transferase
- ☐ Urea

Blood Gases
- ☐ Blood Gas – Arterial
- ☐ Blood Gas – Capillary

Additional Laboratory Tests
- ☐ _____
- ☐ _____

Transitions and Referrals

- ☐ Consult Dietitian re initiation of Parenteral Nutrition
- ☐ Consult Pharmacy
- ☐ Consult _____

Additional Guidelines

Nutrition Practice Guidelines Intravenous Lipid Emulsions- Pediatric
ASPEN Clinical Guidelines: PN Ordering, Review, Labelling & Dispensing 2014
ASPEN Clinical Guidelines: Hyper/Hypoglycemia in Neonates receiving PN 2013

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Appendix A – Adverse Reactions

Appendix A. Potential Allergens in Lipid Solutions

	Peanut	Tree Nuts	Egg*	Soybean	Fish	Shellfish	Olive Oil	Coconut Oil
SMOFlipid®	Yes	No	Yes	Yes	Yes	No	Yes	Yes
Intralipid®	Yes	No	Yes	Yes	No	No	No	No
Omegaven®	No	No	Yes	No	Yes	No	No	No

**Egg allergy: Patients with severe allergic reactions to egg such as anaphylaxis reaction, may need to avoid all types of fat emulsion.*

SMOFlipid®: http://fresenius-kabi.ca/en/wp-content/uploads/sites/2/2013/07/SMOFlipid-PM-En-2015.pdf
Intralipid®: http://fresenius-kabi.ca/en/wp-content/uploads/sites/2/2013/07/Intralipid-PM-ENG.pdf
Omegaven®: http://fresenius-kabi.ca/en/

Appendix B – Estimating Osmolarity of PN Solutions

Appendix B. Approximate Osmolarity of PN Components

PN Component	mOsm/gram	PN Content	mOsm/L
		Example 1 L volume	
dextrose	5	125 g (12.5%)	625
amino acids	10	17 g (1.7%)	170
intravenous lipid emulsion, 20%	1.3 to 1.5 (product dependent)	20 g	30
electrolytes	1 per mEq*	240 mEq	240

* Based on approximation of the osmolarity of the PN component and used as an estimate only
* Calcium, Magnesium 2 mEq= 1mmol, Phosphorus 3 mEq = 1 mmol; Sodium, Potassium, Chloride 1 mEq = 1 mmol

Estimating Osmolarity of PN Solutions *Approximating* the osmolarity of PN: (EXAMPLE)

Consider that:
1. For each 1% dextrose, there are 10 g of dextrose and 50 mOsmol/L
2. For each 1% amino acids, there are 10 g of amino acid and 100 mOsmol/L
3. Therefore:
   In a PN solution with 12.5% dextrose and 17 g amino acids/L
   (or 1.7 g amino acids per 100 mL or 1.7% amino acids),
   there would be:

D12.5W =	12.5 x 50 =	625 mOsm/L
1.7% AA =	1.7 x 100 =	170 mOsm/L
		Total 795 mOsm/L

4. Electrolytes, vitamins and minerals add 300-400 mOsml/L.
5. Intravenous fat is isotonic at about 300 mOsml/L but is not calculated as part of the solution's osmolarity.

Consult Pharmacy for additional information on Osmolarity of PN solutions

Reference:

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Appendix C: General Guidelines for Completing Neonatal Compounded Parenteral Nutrition (PN)

Alberta Health Services

Fluid

PN Volume A
Determine amount of **Total PN Fluid Volume** available
(=TFI-other fluids (IV, enteral, meds))
(mL/kg/day)

→

Amino acid- dextrose solution Volume C
Calculate volume of ***amino acid- dextrose solution*** available
(=PN Volume A – Lipid Volume B)
(mL/kg/day)

→

Calculate **amino acid-dextrose solution infusion rate**
(=PN Volume C x weight(kg) ÷ 24 hr)
(mL/h x 24hr)

Lipid

Choose Intralipid® (default) or SMOFlipid®

→

Determine **amount of lipid** required
(g/kg/day)

→

Lipid Volume B
Calculate **volume of lipid**
(=g/kg/day lipid ÷ % lipid emulsion(20) x 100)
(mL/kg/day)

→

Calculate **lipid infusion rate**
(=PN Volume B x weight(kg) ÷ 24 hr)
(mL/h x 24hr)

Amino Acid-Dextrose Solution

Determine **amount of protein** required
(g/kg/day)

→

Determine **volume of protein**
(=g/kg/day protein ÷ % amino acid(10) x 100)
(mL/kg/day)

Determine **amount of dextrose required**
(g/kg/day)

→

Determine **volume of dextrose required**
(=g/kg/day dextrose ÷ % dextrose(50 or 70) x 100)
(mL/kg/day)

D50 – North and South zones
D70 – Calgary, Central, and Edmonton Zones

→

Pro/Dext Volume D
Combine volume of protein and dextrose
(mL/kg/day)

→

*this is to accommodate additives

Determine Additional Volume
(= ***amino acid-dextrose solution Volume C*** – ***Pro/Dext Volume D***)*
(mL/kg/day)

Energy

Calculate **energy** from **lipid**
(kcal/kg/day)
~10 kcal/g lipid

*Calculate **energy from protein***
(kcal/kg/day)
4 kcal/g protein

*Calculate **energy from dextrose***
(kcal/kg/day)
3.4 kcal/g dextrose

Calculate **amino acid-dextrose energy**
(= energy from protein + energy from dextrose)
(kcal/kg/day)

→

Calculate **Total PN Energy**
(= Lipid Energy + amino acid -dextrose Energy)
(kcal/kg/day)

Function

Determine amount of each electrolyte needed
(mmol/kg/day)

Calgary Zone Only
Also calculate electrolytes as mmol/L

Add **pediatric multivitamin**
2 mL/kg/day

Add **AHS trace element solution**
0.5 mL/kg/day

Preterm Infants need 150+ mcg/kg/day of additional zinc to meet needs

Add **heparin**
0.25 units/mL
amino acid-dextrose solution

Add **levocarnitine**
5-10 mcg/kg/day

Appendix D – Factors Affecting Fluid Requirements in Neonates

Appendix D. Factors Affecting Fluid Requirements in Neonates

Factors that Increase IWL	Factors that Decrease IWL	Other Sources of Fluid Loss	Need for Fluid Restriction	Medication s Altering Fluid Status
Increase activity Respiratory distress Decreased humidity (non-humidified oxygen) Increased ambient temperature Fever (increases fluid needs by 12% per degree Celsius of temperature increase) Tachypnea Extremely low birth weight Metabolic acidosis Cardiac disease Skin breakdown, injury or congenital defects (e.g. omphalocele, gastoschisis) myelomeningocele) Phototherapy and radiant warmer heat may increase losses by 20–40 mL/kg/day	Humidified incubator (decreases IWL by 10–75%) Plastic heat shield with incubator (decreases IWL by 10–30%) Plastic blanket with radiant warmer (decreases IWL by 30–70%) Humidified inspired gas Double-walled incubator Topical agents	Chest tube drainage Ileostomy/fistula drainage High output nasogastric drainage Gastric suction Vomiting Third space loss External ventriculostomy Diarrhea Phototherapy (increases stool H_2O loss) Glusouria (increases urine H_2O loss) High renal solute load (increases urine fluid loss)	Renal failure Congestive Heart Failure Syndrome of Inappropriate antidiuretic hormone (SIADH) with decreased urine output (post-operative status) Meningitis	Diuretics

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Alberta Health Services

Appendix E – Content of Amino Acid Solutions

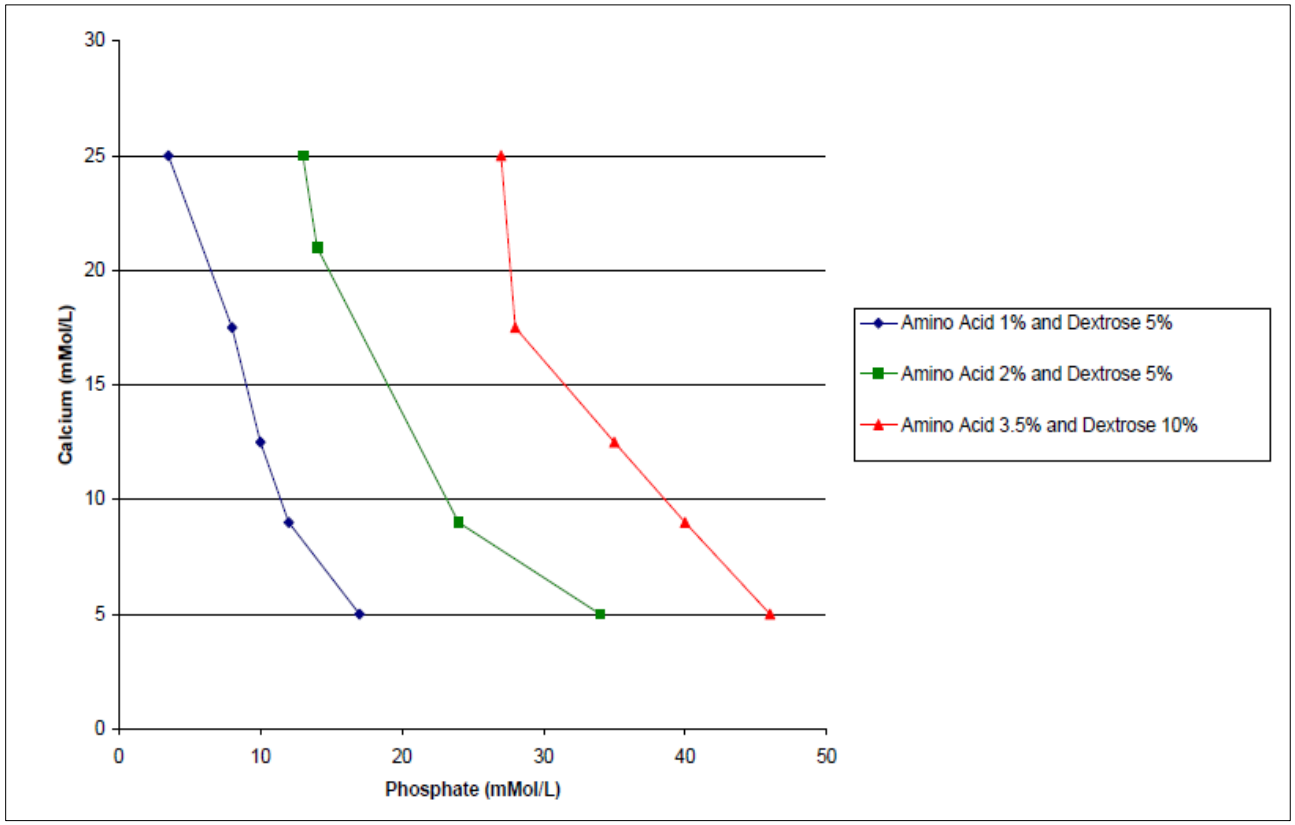
Appendix E. Content of Neonatal Amino Acid Solutions		
Amino Acid mg per 100 mL solution	**Primene™ 10%**	**Trophamine™ 10%**
Essential %	**54**	**60**
Isoleucine – BCAA*	670	820
Leucine – BCAA*	1000	1400
Valine – BCAA*	760	780
Histidine	380	480
Lysine	1100* (as lysine monohydrate)	820 (as lysine acetate)
Methionine	240	340
Phenylalanine	420	480
Threonine	370	420
Tryptophan	200	200
Cysteine	189	Less than 16 (as cysteine HCL H_2O)
Non-Essential		
Glycine	400	360
Alanine	800	540
Arginine	840	1200
Aspartic Acid	600	320
Glutamic Acid	1000	500
Proline	300	680
Serine	400	380
Tyrosine	45	240 (as tyrosine and N-acetyl-L-tyrosine)
Ornithine hydrochloride	318	0
Taurine	60	25
Sodium metabisulfite NF (antioxidant)	0	Less than 50
pH	5.5 with malic acid	5.5 with acetic acid
Osmolarity mOsml/L	780	875
Sodium meq/L	0	5
Chloride meq/L	19 mmol	Less than 3
Acetate meq/L	0	97
** BCAA-Branched Chain amino acids*		

References:

B. Braun Medical Inc. Product monograph: TrophAmine. 2012 November

Baxter Corporation, Clintec Division. Product monograph: Primene. 2015 October

Appendix F – Primene™ Calcium-Phosphate Solubility Curves



**Adapted from the Baxter Corporation April 2016*

Concentrations that fall to the right of the curve may cause precipitation (not all data points were tested.

Appendix G – Assessment of Acid Base Balance

Appendix G. Assessment of Acid Base Balance				
	Definition	**Decreased**	**Normal**	**Increased**
pH	H^+ concentration	Less than 7.35 *acidemia*	7.35 – 7.45	Greater than 7.45 *alkalemia*
pCO_2	Respiratory component of acid-base regulation	Less than 35 mmHg *hypocapnia*	35 – 45 mmHg	Greater than 45 mmHg *hypercapnia*
Base Deficit	Absence or excess buffer in the blood	Less than 4 mmol/L	±4	Greater than 4 mmol/L
HCO_3 –	Metabolic component of acid-base regulation	Less than 18 mmol/L	18 – 25 mmol/L	Greater than 25 mmol/L
* *Adapted from ACoRN Manual, Solimano A, 2009 1st Edition*[60]				
* *pH and PCO²targets may differ based on the neonate's clinical status and organ function.*				

Stepwise Assessment of Acid Base

1. Assess pH – is this alkalemia or acidemia?
2. Assess pCO_2 and HCO_3^- – is this metabolic or respiratory?
3. If acidemic, calculate anion gap. This will determine treatment path.
   a. Anion gap = $Na^+ – (Cl^- + HCO_3^-)$ = 3 – 11 mEq/L
4. Determine if disorder is acute (<48h) or chronic (>48h).
5. Determine if compensation has occurred. If kidneys or lungs have compensated by normalizing pH the cause of the underlying disturbance will still need to be treated.

Appendix H – Interpretation of Acid Base Balance

Appendix H. Interpretation of Acid Base Balance

pH	pCO_2	Base	HCO_3^-	Increased	Compensation	Common Causes
Decreased	Increased	Normal	Normal	Respiratory acidosis	Kidneys (excrete H^+ and retain HCO_3^-)	Insufficient respiratory rate/drive, airway obstruction, inadequate ventilation, lung injury or disease (RDSoverfeeding hypophosphatemia, CNS depression (HIE, hemorrhage, narcotics)
Decreased	Normal	Deficit	Decreased	Metabolic acidosis	Respiratory (increasing resp. rate to decrease PCO_2)	Non anion gap: excessive HCO_3^- loss (vomiting/GI losses, diarrhea/ostomy, renal), hypochloremia, Anion gap: renal failure, ketoacidosis, lactic acidosis secondary to poor perfusion /hypotension/sepsis
Increased	Decreased	Normal	Normal	Respiratory alkalosis	Kidneys retain H^+ and excrete HCO_3^-)	Hyperventilation, hypoxia, severe anemia
Increased	Normal	Excess	Increased	Metabolic acidosis	Respiratory (hyperventilatio n to increase PCO_2)	Saline responsive: cystic fibrosis (chloride loss), diuretics, excessive bicarbonate intake or acetate in TPN, gastric losses Saline resistant: corticosteroid use

Appendix I – Trace Element Roles – Signs of Deficiency and Toxicity

Appendix I. Summary of Trace Element Roles – Signs of Deficiency/Toxicity

Mineral	Role	Cause of deficiency	Signs of deficiency	Signs of Toxicity	Special Considerations	Lab Test
Selenium [2,3,4,5,6,7,8,9,10]	Essential trace element Protects against membrane oxidative damage Free radical scavenger Cofactor in antioxidant enzymes	Cardiomyopathy Stress Infection Vitamin E deficiency Skeletal muscle disorders Erythrocyte macrocytosis Conditions prone to deficiency Malabsorption high GI losses, fistula CRRT*	Fingernail bed abnormalities Growth impairment Alopecia Pseudoalbinism	Oxidative damage to cells and tissue Loss of hair and nails Fatigue Irritability Peripheral neuropathy	Increased needs during prolonged inflammation Observed geographic low SE soil, long-term PN, low protein diets, malabsorption Serum selenium is a negative acute phase reactant	Serum Selenium
Zinc [2,3,5,8,11,12]	Cofactor in metalloenzymes involved in protein, fat, carbohydrate metabolism, growth and cell differentiation Hormone structure GI development Immune function Genetic transcription Heme, LCFA* and prostaglandin synthesis	Severe diarrhea Inflammatory/malabsorptive disorders Abnormal fluid losses (stomas, fistulas, bilious gastric drainage) High urinary output post-surgery or with high output renal failure	Poor growth Periorificial dermatitis Glossitis Increased Infections Impaired wound healing and immune function	Decreased absorption of copper and iron Macrocytosis Neutropenia Decrease HDL Impaired immune function Diarrhea	Increased needs with: Severe diarrhea Inflammatory/ malabsorptive disorders Abnormal fluid losses (stomas, fistulas, bilious gastric drainage High urinary output post-surgery or with high output renal failure Serum zinc Low levels may not occur until deficiency is severe Negative acute phase reactant	Serum zinc

Zinc cont… [2,3,5,8,11,12]	Cholesterol transport Cell membrane stabilization Zinc is bound to albumin					
Copper [2,13,14,15]	Antioxident functions protect cell membranes from oxidative damage Component of many metalloenzymes affecting many metabolic process Ceruloplasmin is the major plasma Cu transporter – releases iron from hepatic stores Collagen/bone formation Neuropeptide synthesis	High enteral Zn/Fe compete for Cu absorption Increased biliary losses Conditions prone to deficiency Prolonged GI losses	Anemia resistant to Fe Pancytopenia/neutropenia (initial sign) Osteoporosis osteopenia Poor wound healing Neurological abnormalities	Accumulation in liver, kidney and brain leading to organ failure	Needs may be decreased in cholestasis Caution in impaired biliary excretion since 80% of PN copper is excreted in bile Increased needs with biliary losses (consider increase of 10-15 mcg/kg Since ceruloplasmin is an acute phase reactant, it may be high when inflammation present even in Cu deficiency	Serum copper and ceruloplasm
Iron [5,13,14,15,16]	DNA replication Cellular energetics Oxygen delivery Neurodevelopment T-cell immunity	Blood loss Long term PN without adequate supplementation	Anemia Lethargy Impaired immune function Failure to thrive Motor/cognitive developmental delays Impaired temperature regulation Glossitis	Accumulation in liver, pancreas, heart leading to tissue damage Increased oxidative injury (and possible increased risk of BPD/ROP* in premature infants Increased risk of infection	Decreased needs with blood transfusions Increased needs with blood loss and erythropoetin treatment (up to 3mg/kg/day)	Iron studies: Ferritin, TIBC*, iron, % saturation

Manganese [2,3,5,8,13,15,17]	Enzyme cofactor (SOD/PC*) High concentrations in liver and brain Cellular defense against free oxygen radicals Bone formation	Rare	Affects muco/lipo-polysaccharide formation Rare Altered protein synthesis	Neurotoxicity Extrapyramidal neurological disease Hepatic complications	Not in provincial AHS PN trace element solution Omit in cholestasis, impaired biliary excretion Possible contaminant in multiple PN ingredients	Serum Manganese
Molybdenum [2,3,5,8,13,15]	Enzyme cofactor High concentrations in liver and brain Cellular defense against free oxygen radicals Bone formation	Rare in neonates	Tachycardia Neurological symptoms Lethargy Nausea/vomiting	Rare	Present as a contaminant in PN solutions	Not done in AHS
Chromium [2,3,58,13,15,18]	Metabolism of protein, carbohydrate, fat Potentiate action of insulin Glucose tolerance	Long term PN	Weight loss High plasma FFA concentration Glucose intolerance	Reduced glomerular filtration rate Renal tubular damage	May omit in short-term PN Contaminant in multiple PN ingredients Decrease dose in renal impairment	Serum Chromium
Iodine [2,3,5,19]	Thyroid function involved in metabolism of protein and energy Growth development, maturation		Hypothyroidism Deafness Mental retardation Increased perinatal and neonatal mortality	Hypothyroidism with signs of goiter or hyperthyroidism	Small enteral intake or iodine disinfectants likely meeting basal needs Extremely preterm neonates and those with SBS* may need more iodine than the provincial trace element solution provides	Urine Iodine Thyroid function (T3)

**LCFA – long chain fatty acid, CRRT – continuous renal replacement therapy; SOD superoxide dismutase; BPD – broncoiopulmonary disease; ROP – retinopathy of prematurity; TIBC – total iron building capacity; PC – pyruvate private carboxylase; SBS – short bowel syndrome*

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Appendix J – Vitamin Roles – Signs of Deficiency and Toxicity

Appendix J. Summary of Vitamin Roles – Signs of Deficiency/Toxicity [1.2]

Vitamin	Role	Cause of deficiency	Signs of deficiency	Signs of Toxicity	Special Considerations	Lab Test
Vitamin B_1 (Thiamine)	Carbohydrate and energy metabolism	Thiamine free PN Refeeding syndrome/ malnutrition Loop diuretics CRRT* Gastric Surgery	Wernicke encephalopathy /infantile beriberi May lead to: Inadequate ATP synthesis Abnormal carbohydrate metabolism Deficiencies of other B vitamins	Not reported	Increased needs due to: Fever Infection Hyperparathyroidism High carbohydrate intake Malabsorption disorders Additional is compatible with PN however can also be provided separately	Not available in AHS
Vitamin B_2 (Riboflavin)	Catalyst in reduction/oxidation reactions Energy metabolism B vitamin metabolism	Malabsorption SBS* Catabolism and certain medications increase urinary excretion Thyroid dysfunction Usually occurs in conjunction with multiple nutrient deficiencies	Increased glutathione reductase activities Deficiencies of other B vitamins Pharyngitis, cheilosis, angular stomatitis glossitis Seborrheic dermatitis, edema of pharyngeal and oral mucosa Corneal changes	Photo oxidization of some amino acids Rare	Losses with clear tubing	Not available in AHS
Vitamin B_3 (Niacin) [3.4]	Energy metabolism	Malabsorption	Pellagra, diarrhea, dermatitis	Vasodilatory (flushing),	Flushing may be improved by slowly	Not available in AHS

Vitamin B_3 cont… (Niacin) [3,4]	Synthesis of fatty acids and steroids DNA replication Repair and cell differentiation	Decreased conversion of tryptophan to niacin as seen in excess leucine uptake	Thyroid dysfunction Deficiencies of B vitamins Glossitis, angular stomatitis, chelitis	nausea/vomiting, hepatitis, neuro-visual disturbances, glucose intolerance	increasing dose, taking dose with food and using a slow release form of supplement	
Vitamin B_6 (Pyridoxine)[5,6]	Cofactor for enzymes involved in amino acid metabolism	Malabsorption	Seizures Deficiencies of other B vitamins Dermatitis Microcytic anemia Angular stomatitis, glossitis, cheilosis	Peripheral sensory neuropathy Skin lesions		Not available in AHS
Folic acid[7,8]	DNA synthesis Amino acid interconversions	Malabsorption SBS – duodenum, jejunum Impaired metabolism Inadequate intake CRRT*	Seizures, neuromotor disorder, developmental delay, megaloblastic anemia Diarrhea Decreased immune function	Exacerbates B_{12} deficiency neuropathy Seizures	Additional is compatible with PN	Serum Folate Plasma homocysteine
Vitamin B_{12} (Cyano-cobalamine) [9,10,11]	Conversion of homocysteine to methionine and DNA synthesis Fatty acid metabolism	Resection of stomach, terminal ileum Lack of pancreatic exocrine function or intrinsic factor Bacterial overgrowth Breastfed neonates of strict vegan mothers	Macrocytic megaloblastic anemia, involvement of nervous system	Rare Cyanocobalamin worsens Leber's optic atrophy, use hydroxycobalamin		Serum B_{12} Mean corpuscular volume MMA (most sensitive measure)

Vitamin B_5 (Pantothenic Acid)	Metabolic reactions Fatty Acid synthesis	Malnutrition Deficiency occurs in combination with other B vitamins deficiencies	Gastrointestinal and nervous system	Not reported		Not available in AHS
Biotin [12, 13,14]	Fatty acid elongation TCA cycle (gluconeogenesis)	Biotin free PN Genetic biotinase deficiency (neonate)	Infantile seizures developmental delay, rash (around mouth, nose eyes) alopecia Dermitis Hypotonia	Not reported		Not reported in AHS
Vitamin C (Ascorbic Acid) [15]	Hydroxation of collagen Biosynthesis of carnitine, peptide hormones and tyrosine metabolism	Severely restrictive diets Trauma, burns, surgery Wounds, pressure ulcers CRRT*	Scurvy Weakening of collagenous structure Bleeding gums Petechiae Impaired wound healing Anemia	Rare Nausea, abdominal cramps, diarrhea	Losses with clear tubing Serum ascorbic acid is falsely lowered in the acute phase response to illness Additional not compatible with PN as high doses can cause a more acidic solution and increase risk of oxalate stone formation with calcium	Serum Ascorbic Acid
Vitamin A (Retinol) [16,17]	Vision Epithelial integrity Gene expression Protects against BPD	Preterm neonates: Low body stores Increase losses in delivery system Inadequate intake Defective intestinal delivery due to	Xerophthalmia Night blindness Impaired wound healing Bitot's spots	Renal dysfunction (reduced retinol binding protein) (RBP) renal clearance) Liver disorders PN amount Neonates	Preterm neonates born with low body stores Increased losses in delivery system Routine measures not required when receiving parenteral vitamin A	Serum retinol+/- RBP

Vitamin A (Retinol) [16,17] cont…		Immature abnormal hepatobiliary function Damaged epithelial integrity Malabsorption Other Impaired mobilization from the intestine or liver PN exposed to light Absorbed onto glass and plastic		Bulging fontanelle (ICP) Craniotabes Hypercalcemia Hyper-phosphatemia Metastatic calcifications	May have adequate vitamin A stores in the liver but low serum vitamin A levels due to low RBP	
Vitamin D (Alfacalcidol) [19,20,21]	Maintain normal serum calcium levels Bone formation and maintenance	Cholestasis Liver dysfunction Renal failure Seizure medications Inadequate intake	Rickets Hypocalcaemia Ostomalacia Osteoporosis Associated with metabolic bone disease in long-term PN	Hypervitaminosis D from excess intake leading to hypercalcemia (polyuria, polydipsia, depression, metastatic calcification of soft tissues	PN less than 4 weeks: no indication for routine monitoring Long term PN greater than 4 weeks, monitor levels yearly in conjunction with serum magnesium, calcium phosphate, and parathyroid hormone (PTH)	Total serum 25-hydroxy vitamin D Serum 1, 25-dihydroxy vitamin D
Vitamin E (Alpha tocopherol) [22,23]	Fat soluble antioxidant	Prolonged steatorrhea SBS Severe malnutrition Liver dysfunction	Increased infections Anemia Growth stunting Peripheral neuropathy Increase platelet aggregation	LBWI with elevated vitamin E (greater than 5.1 mg/day) have increase incidents of sepsis and necrotizing enterocolitis	Routine monitoring not required while on PN	Serum vitamin E

Vitamin E (Alphatocopherol) [22,23] cont…		Systemic inflammatory response, multi-organ failure Omega 3 fatty acid supplementation	Axonal neuropathy			
Vitamin K_1 (Phytonadione) [16,24]	Clotting function	Malabsorption SBS Cholestasis Renal Failure Chronic antibiotics	Increased Prothrombin time Hemorrhage if severe	Rare	Large amounts of PN vitamin K associated with hemolytic anemia, hyperbilirubinemia, kernicterus, liver damage and anaphylaxis Additional is compatible with PH Intravenous lipid emulsions (ILE) contains inherent amounts of vitamin K	Prothrombin time, (PT/INR)

* SBS – short bowel syndrome; MMA – methylmalonic academia; TCA – tricarboylic acid; LBWI – low birth weight infant; INR – international normalizing ratio

*For zone specific information on blood draw protocols, guidelines and pediatric reference intervals, refer to Laboratory Test Directory and Collection information located at http://www.albertahealthservices.ca/lab/page3217.aspx.

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Appendix K – Metabolic Complications

Appendix K. Metabolic Complications

Complication	Possible Causes	Treatment/Prevention
Glucose Metabolism		
Hyperglycemia (may be associated with glycosuria, osmotic diuresis, hyperosmolar dehydration, chronic lung disease, retinopathy of prematurity, increased morbidity and mortality, steatosis, NEC, intracranial hemorrhage or coma)	• Excessive rate or amount of dextrose infusion • Inadequate endogenous insulin • Glucocorticoids • Sepsis • Renal disease • Thiazide diuretics	• Decrease dextrose provided; however, continue to provide a minimum GIR of 4 mg CHO/kg/min. Evaluate for sepsis and treat if necessary.
Hypoglycemia (post infusion)	• Increased insulin production • Hepatic glycogenic enzyme immaturity • Interrupted or too-rapid weaning of dextrose solution	• Carefully taper infusion rate when weaning • If parenteral nutrition is interrupted, infuse an appropriate dextrose in water solution (example: D10W). Monitor serum glucose.
Amino Acid Metabolism		
Hyperammonemia	• Liver disease or hepatic immaturity • Inborn errors of protein metabolism	• May need to decrease protein intake. • Monitor serum ammonia and serum prealbumin.
Pre-renal azotemia	• Excessive protein infusion, especially in LBW infants or inappropriate calorie: protein ratio • Intravascular volume depletion • Dehydration • Catabolism	• Lower protein intake. • Achieve total calorie: protein ratio of 25 – 40 kcal: 1 gram of protein. • Monitor BUN, creatinine and albumin. Note: BUN may be elevated in the first 2 weeks of life during high protein turnover and lean muscle accretion. • Ensure proper hydration of patient.
Lipid Metabolism		
Essential fatty acid (EFA) deficiency	• Inadequate EFA (linoleic acid) administration • Fat-free TPN	• Requirements can be met by providing Intralipid® at 1 g/kg/d (preterm) and 0.5 g/kg/d (term) **or**

Essential fatty acid (EFA) deficiency cont…	• Omegaven® use	SMOFlipid® at 1.3 g/kg/d (preterm) and 0.6 g/kg/d (term). • Monitor triene: tetraene ratio. It can take an extended period of time to receive results for the triene: tetraene ratio and therefore it may not be a realistic monitoring tool if the patient is on short term PN.
Hypertriglyceridemia and high levels of free fatty acids	• Rapid infusion or high dose of intravenous lipid emulsion • Stress and/or inflammation • Infection • Prematurity • Excessive dextrose intake • Medications e.g. cyclosporin, tacrolimus, sirolimus	• Slow/decrease administration of intravenous lipid emulsion as necessary to maintain TG in acceptable range (less than or equal to 2.8 mmol/L) • Monitor serum triglycerides.
Hyperbilirubinemia (nutrition-related)	• Potential displacement of bilirubin from albumin binding sites by high serum free fatty acid levels	• Monitor serum bilirubin and triglycerides, maintaining triglycerides at less than 2.8 mmol/L
Hepatic Metabolism		
Hepatic dysfunction or hepatic failure	• Dextrose, protein, fat, and vitamin components have been implicated, but studies are inconclusive • May be due to sepsis, prematurity, ischemia, or postoperative status • Lack of enteral feeding resulting in decreased bile flow	• If there is no other means of nutritional support, continue PN, adjusting solution on an individual basis. • Avoid overfeeding and provide balanced PN. • If standard crystalline amino acid (CAA) solution is being infused, change to a neonatal CAA solution. • Shield PN from light to prevent vitamin deterioration and lipid peroxidation. • Start enteral feedings as soon as possible. • Rule out infection and other causes of hepatic dysfunction. • Monitor liver function weekly and serum copper as needed. • Consider using SMOFlipid®
Mineral & Electrolyte Metabolism		
Electrolyte imbalances	• Renal tubular dysfunction • Immature kidney	• Electrolyte losses should be measured and replaced.
Hyperphosphatemia	• Excessive intake • Decreased renal function or parathyroid hormone (PTH) deficiency	• Decrease phosphorus intake. • Monitor calcium and phosphorus.

Hyperphosphatemia cont…	• Vitamin D excess • Medications • Hypocalcemia • Hypoparathyroidism • Acidosis • Rhabdomyolysis	
Hypophosphatemia	• High dextrose infusions • Inadequate phosphorus administration • Metabolic acidosis • Malnutrition/malabsorption • Rapid refeeding • Rapid growth • Corticosteroids	• Increase phosphorus intake • Monitor phosphorus and calcium
Hypocalcemia	• Inadequate calcium intake • Previous increase in phosphorus intake • Diuretic administration (furosemide) • PTH deficiency • Inadequate magnesium intake • Vitamin D deficiency/ malabsorption • Corticosteroids • Using citrate to treat metabolic acidosis may increase urinary calcium excretion	• May begin calcium replacement using separate IV line (do not mix with TPN to avoid precipitation). • Increase calcium content of solution
Hypercalcemia	• Increased calcium intake • Inadequate phosphorus intake • Excess vitamin D • Magnesium deficiency • Hyperparathyroidism • Metabolic acidosis	• If needed, decrease calcium content of solution and/or increase phosphorus content. • Monitor ionized calcium, phosphorus, vitamin D, PTH • Often considered a medical emergency and may require consultation from endocrinology, cardiology and nephrology
Hypomagnesemia	• Inadequate magnesium administration relative to increased requirements for protein anabolism and dextrose metabolism • Malabsorption or excess losses (chronic diarrhea) • Medications e.g. amphotericin B, cyclosporin, tacrolimus, diuretics • Hypercalcemia • Hypophosphatemia	• Increase magnesium content of solution • Monitor serum magnesium, calcium, and phosphorus
Hypermagnesemia	• Excessive magnesium administration • Severe trauma • Renal failure • Recent maternal MgSO4 administration • Severe dehydration • Rhabdomyolysis	• Decrease magnesium content of solution. • Monitor serum magnesium, ionized calcium and phosphorus as they are all renally excreted.
Hyponatremia	• Diuretic medications (e.g. furosemide) • H2 antagonists • Over-hydration	• Gradually increase sodium content of solution to avoid increasing the risk of IVH.

Hyponatremia cont…	• Excessive losses • Immature kidney function • Treatment of patent ductus arteriosus with indomethacin causes water retention	• Replacement equation for Na deficit in acute hyponatremia. • Dose in mmol= Wt (kg) x 0.8 x (CD - CA) CD = desired serum Na concentration in mmol/L and CA = infants actual, current Na concentration in mmol/L. • See pharmacy monograph of sodium supplementation for further details. • Monitor serum sodium.
Hypokalemia	• Inadequate potassium administration relative to increased requirements for protein anabolism • Medications (e.g. potassium depleting diuretics, amphotericin B, corticosteroids) • Excess GI losses • Metabolic alkalosis	• Increase potassium content of solution. • Monitor serum potassium.
Hyperkalemia	• Excessive potassium administration • Metabolic acidosis • Renal failure/obstruction • Medications (e.g. cyclosporin, tacrolimus, potassium sparing diuretics) • Hemolysis • Intraventricular hemorrhage (IVH) • Non-oliguric hyperkalemia (NOHK)	• Decrease potassium content of solution. • Monitor serum potassium. • Use of insulin may be considered
Hypochloremic alkalosis	• Too much acetate and too little chloride in solution • Diuretics • Metabolic alkalosis 2^{o} severe loss of body fluids	• Increase chloride content and decrease acetate content of solution. • Monitor serum chloride and bicarbonate.
Metabolic Bone Disease (MBD)		
Osteomalacia, osteopenia, osteoporosis	• Long-term PN • Medications • Calcium, phosphorus and vitamin D deficiencies/ malabsorption • Metabolic acidosis • High aluminum contamination in PN • Excessive vitamin D	• Monitor alkaline phosphatase, serum phosphorus, ionized calcium. • Optimize parenteral calcium and phosphorus while providing parenteral vitamin D. • If low PTH and 1,25 hydroxyvitamin D with normal 25 (OH) Vit D, with MBD remove vitamin D from PN. • In patients on long-term PN with unexplained MBD, check serum aluminum level (if able) as aluminum may result in poor rate of bone formation.

Appendix L – Cholestatic Liver Disease

Guidelines for PN in Infants with Cholestatic Liver Disease

- Preterm infants with cholestasis requiring PN > 1month should have serum copper checked at 4 weeks after PN initiation and then monthly. If levels are normal, continue with current trace solution. If levels are high, stop the current trace element solution and dose trace elements separately decreasing copper to10 mcg/kg/d or hold the dose and continue to monitor levels. Refer to copper section on page 25.
- Trophic feeds will stimulate bile flow, promote intestinal maturation and stimulate enteral hormones.[41, 101]
- In small infants continuous dextrose infusion is critical in the setting of end stage liver disease because of reduced glycogen stores. Hypoglycemia can develop within 30 minutes of stopping dextrose infusion in infants who have poor glycogen stores and increased metabolic demands due to end stage liver disease.[101]
- Meet calorie need while maintaining euglycemia and using well-balanced PN solutions ensuring no overfeeding.[132] Refer to ***Section 3.2 – General Guidelines for PN Prescription***.
- The medical team may prescribe ursodeoxycholic acid in order to stimulate bile flow if receiving enteral feeds.[8] Additional vitamin supplementation is required once enteral feeds are established.

Cyclic PN for the treatment of cholestatic liver disease in the neonatal population remains controversial.

Appendix M – Refeeding Syndrome

- Placental insufficiency leads to a state of chronic malnourishment and altered oxygen delivery to the fetus. Additional calories and protein intake provided in the first week of life to very-low-birth-weight intrauterine growth-restricted neonates (Less than 1500 grams) may induce electrolyte imbalances (hypophosphatemia, hypokalemia, hyperglycemia, hypomagnesemia and hypercalcemia), similar to laboratory markers of refeeding syndrome.
- Phosphate supplementation may be delayed in the first 72 hours of life as the parenteral solution may not contain sodium and potassium due to the infants immature kidney function.
- Early amino acid intake in premature infants is associated with increased endogenous insulin production. Intracellular shifts of phosphate and potassium occur for energy production along with synthesis of glycogen, fat and protein. Excessive glucose metabolism results in increased phosphate usage for ATP production, further depleting phosphate stores.
- Severe hypophosphatemia may inhibit chemotaxis, initial phagocytosis and bactericidal activity, further increasing the infants risk for septicemia.
- Close monitoring of electrolytes, especially phosphorous, is warranted following initiation of parenteral and enteral nutrition in the IUGR population. Earlier administration of phosphorous and potassium, may decrease the incidence of electrolyte abnormalities.

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